HEART DISEASE

Its Diagnosis and Treatment

BY

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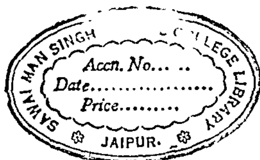
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veratrum viride and the ganglionic blocking agents such as methonium. The treatment of atherosclerosis with low-fat, low-cholesterol diets and lipotropic agents has been described in detail in a new chapter

The entire subject of acute and chronic cor pulmonale has been rewritten, with emphasis on treatment New material on amniotic fluid embolism, bone marrow embolism, pulmonary emphysema, pulmonary fibrosis, and oxygen poisoning, has been included.

Vascular lesions, such as thrombosis of the internal carotid artery, and thrombotic occlusion of the abdominal aorta (the Leriche syndrome) are described New methods of diagnosing and treating adrenal diseases are included A chapter on the kidney and heart disease has been added. In addition, several hundred new references have been added to keep the bibliography complete and up-to-date.

Although I have tried to present all points of view when discussing controversial subjects, such as mitral valve surgery, I have not hesitated to express my own opinion, and have continued to state my preference for particular methods of treatment, when I felt that such an opinion would be helpful to the practicing physician

I should like to express my appreciation to Dr Louis Leiter, Chief of the Medical Divison of Montefiore Hospital, for his helpful suggestions

I should also like to express my appreciation to my many good friends who have been helpful, especially to Herbert F. McAuliffe and Thelma Goldberg, for help with the proofreading, and to David M Harris, for help in reproducing the new illustrations. My wife, as usual, has been of inestimable help

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From a functional point of view, similar deductions can be made. The hyperpnea, dyspnea and cyanosis bespeak pulmonary congestion, and this in turn can be assumed to be due to left-sided heart failure. The distended neck veins with systolic pulsations and the large liver indicate right-sided heart failure. Even the arrhythmia can be predicted, because the most common cause of a radial pulse and an apical heart beat, completely irregular in rate, and rhythm and force of contraction, is auricular fibrillation, normal electrokymographic and electrocardiographic patterns, and normal values for tests of circulatory efficiency (venous pressure, circulation times cardiac output, venous catheterization studies, *etc.*)

So that, despite the fact that we have not taken a history or even placed a stethoscope on the patient's chest, we can assume, as a working hypothesis that the patient has long-standing rheumatic heart disease, with mitral stenosis and auricular fibrillation, and is in both right- and left-sided heart failure, which probably was the cause of her hospitalization.

Is it possible that this is not the correct diagnosis? Yes. Shall this be the extent of the cardiac examination? Of course not. Shall the stethoscope be used and other diagnostic procedures done? Certainly, but I have described this case to emphasize that the doctor should always remember that within himself lie great diagnostic potentialities.

A few words should be written about the plan of this book It has been divided into five main sections: Section I describes the normal heart, including normal physical signs, normal fluoroscopic and *x*-ray findings, normal electrocardiographic patterns, and normal values for tests of circulatory efficiency (venous pressure, circulation times, cardiac output, venous catheterization studies, *etc.*)

Section II describes the abnormal heart, including symptoms referable to the cardiovascular system, abnormal physical signs, abnormal findings on fluoroscopic and *x*-ray examination, abnormal electrocardiographic patterns, and abnormal findings in tests of circulatory efficiency.

Section III describes the cardiac syndromes of congestive heart failure, shock, syncope and related states, the anginal syndrome, neurocirculatory asthenia, and the cardiac arrhythmias and bundle branch block.

Section IV is devoted to a systematic description of cardiac abnormalities based in general on an etiological classification, *viz:* congenital heart disease, rheumatic heart disease, hypertensive heart disease, *etc.* However, certain diseases of varying etiology but of common anatomical abnormality, such as diseases of the pericardium, diseases of the aorta, *etc.*, have been described together in order to emphasize the characteristic clinical pictures which these conditions present.

Section V describes special conditions complicating heart disease, such as pregnancy, surgery and anesthesia, and the general problem of employment of the cardiac.

Although physical diagnosis has been
diagnosis have not been neglected, and
general plan has been used: classificati

ogy, etiology, symptoms, physical signs, fluoroscopic and x-ray examination, including angiocardiography, roentgenkymography and electrokymography, electrocardiogram, laboratory tests, including venous pressure, circulation times, cardiac output, venous catheterization studies, *etc.*, diagnosis, course and prognosis, and treatment. I have also separately described normal and abnormal findings and treatment for infants and young children.

In describing rare conditions, I have paid special attention to those lesions, such as tricuspid atresia, double aortic arch and other vascular rings around the trachea and esophagus, *etc.*, which are now amenable to surgical therapy. X-ray illustrations and electrocardiograms have for the most part been reproduced diagrammatically to illustrate more clearly basic patterns. References have been appended at the end of each chapter, appropriately divided by subject matter. The bibliography is representative rather than exhaustive, and I have emphasized easily accessible references in the English language. The titles of all papers have been included to help the inquiring reader refer to material described in the text.

I should like to express my appreciation to Dr. Louis Leiter, Chief, Medical Division, and to Dr. E. M. Bluestone, Medical Director, Montefiore Hospital, New York, for their cooperation; to Dr. Solomon Fineman, Attending Roentgenologist, and to Dr. Joel J. Schwartzman, Associate Attending Roentgenologist, Montefiore Hospital, for permission to reproduce the x-ray films. I am also indebted to my colleagues at Montefiore Hospital with whom I am associated in the post-graduate cardiology teaching program of Columbia University, for the constant intellectual stimulation I have derived from them.

In am deeply indebted to Majorie Lave Margulies, my capable medical artist, whose illustrations adorn the book. I also wish to thank my good friend, Herbert F. McAuliffe, for his help with the proofreading. And I am extremely indebted to my wife for her constant encouragement and help in the preparation of the manuscript.

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Heart Disease

Section 1. The Normal Heart

Chapter 1

PHYSICAL EXAMINATION OF THE CARDIOVASCULAR SYSTEM

BLOOD PRESSURE DETERMINATION

Having the blood pressure taken has become a fetish to many a patient who follows the fluctuations in his pressure with the intense interest of the stock market speculator watching the ticker tape None the less, blood pressure readings have value

Arterial blood pressure, or blood pressure, to use its common name, can be defined as the lateral pressure exerted by the column of blood against the arterial walls With systole, the pressure rises to a level which depends on the force of contraction of the heart, the elastic resistance of the arteries, the quantity of blood in the arterial system, the peripheral resistance, and to a lesser extent, the viscosity of the blood The level of the blood pressure during diastole is determined to a large extent by the elastic recoil of the arteriolar walls

With each systole, about 60 cc of blood is forced into the aorta, which contains considerable blood even during diastole. This distends it still further A moment later, the elastic recoil of the aortic wall drives on the blood, which distends the next segment of arterial wall In this way the wave of distention is transmitted with gradually decreasing force along the arterial tree This wave of distention is what we feel when we take the pulse

As the contractile wave spreads away from the heart to the smaller arteries, the pressure in the arterial system falls in a gradual slope because part of the energy from the heart is dissipated in overcoming friction. The fall in pressure from the aorta to the smaller arteries is about 20 mm. of mercury, but the friction encountered in the passage of the blood through the arterioles causes another drop of 50 to 60 mm By far the greater part of the peripheral resistance of the circulatory system occurs in the arterioles of the abdominal organs, the so-called splanchnic area (This is one of the reasons that sympathectomy has been recommended in selected cases of hypertension—the section of the sympathetic fibers decreases the resistance of the splanchnic arterioles.

Beyond the arterioles, the blood flows slowly through the extremely large capillary bed and through the veins to the right auricle, and the pressure falls still further, so that by the time the blood has reached the right auricle the pressure is almost zero

Methods of Determining Blood Pressure. –Arterial blood pressures cannot be measured precisely with a sphygmomanometer because comparison of values so obtained with those measured directly with an intra-arterial manometer reveals that the pressures recorded with the sphygmomanometer are in error about plus or minus 8 mm Hg Despite this, the sphygmomanometer is very useful clinically

In order to establish a uniform method of obtaining blood pressure readings, the Council for High Blood Pressure Research of the American Heart Association has published the following suggestions

The sphygmomanometer may be mercurial or aneroid, but an aneroid instrument, if used, should be calibrated at least yearly against a mercurial instrument.

The inflatable cuff, roughly speaking, should be 20 per cent wider than the diameter of the arm or thigh on which it is to be used. Bags having the following widths are commercially available: for thighs of adults, 18 cm , for arms of adults, 12 cm. A length of bag sufficient to half encircle a limb is adequate, provided care is taken by the operator to place it on the side of the compressible artery However, some authorities believe that any risk of misapplication should be obviated by use of a bag that nearly or completely encircles a limb

Technic. –The patient may be either in a recumbent position or comfortably seated He should be placed at ease and time should be allowed for recovery from any unusual recent exercise, meals, or apprehension The arm should be bared, slightly flexed, abducted, and perfectly relaxed. In the sitting position, the forearm should be supported at heart level on a smooth surface. The hand may be pronated or supinated later, depending on which position is found to yield the clearest sounds The deflated bag and cuff should be applied evenly and snugly around the arm with the lower edge about 1 inch above the antecubital space. If the veins of the forearm are prominently filled or if there is evidence of congestion, the cuff should be applied while the arm is elevated in order to promote venous drainage.

General Precautions.—The mercury column must be vertical. The meniscus should be read at a level with the observer's eye. It is not important to place the manometer at the heart level

Determination of Systolic Pressure by the Palpatory Method —A comparison of systolic pressure by the palpatory and auscultatory methods is always advisable except in infants in which the former method alone is usually done. *The patient's radial pulse should be palpated and its rate and regularity* estimated and recorded The pressure of the cuff should be raised to about 30 mm. of mercury above the point at which the radial pulse disappears. Pressure should then be released slowly at such a rate that *pressure in the manometer falls about 2 to 3 mm. Hg per heart beat.* The return of palpable beats should be noted as a preliminary estimate of systolic pressure. The cuff should be rapidly and completely deflated before further determinations are made.

Determination of Systolic Pressure by the Auscultatory Method.—A stethoscope receiver should be applied snugly over the brachial artery in the antecubital space, free from contact with the cuff. The pressure in the sphygmomanometer should then be raised rapidly above the estimated systolic blood pressure level; and then decreased slowly, as in the palpatory method, until a sound is heard with each heart beat. This reading is noted as the systolic pressure.

As a rule, the systolic pressure determined by the auscultatory method is higher than the pressure at which radial pulse beats are first palpable. In case the palpatory reading should be higher than the auscultatory, the following may be done to improve conditions for hearing the sounds:

Avoidance of Congestion in the Arm Veins.—Congestion nullifies the auscultatory criteria both by lowering the level at which sounds appear and by causing them to drop out when the cuff pressure is between systolic and diastolic. (This phenomenon, in which the usual sounds are heard over the brachial artery at a fairly high level but disappear as the pressure in the cuff is reduced, only to reappear at a much lower level, is known as the **auscultatory gap**. This is the reason that the palpatory method of obtaining the systolic pressure should always be used as a check on the auscultatory method.)

If, despite such an effort, the pressure obtained by palpation continues to be higher, it should be accepted as the reading for systolic pressure.

Determination of Diastolic Pressure by the Auscultatory Method.—With continued deflation of the cuff below systolic pressure at a rate of 2 to 3 mm. Hg per heart beat, the sounds undergo changes in intensity and quality. As the cuff pressure approaches diastolic, the sounds often become dull and muffled quite suddenly and finally cease. *It is recommended that the point of complete cessation is the best index of diastolic pressure.* (If the point of muffling of the sounds [the fourth phase of Korotkoff] is used as the diastolic pressure, the values obtained will be 5 to 10 mm. above this level.)

Diastolic pressure values are more important than systolic pressure values because the diastolic pressure represents the constant load which the vascular walls are carrying, not only in the larger vessels but *throughout the arterial system.* This is so because the systolic pressure falls considerably from the aorta to the smaller peripheral arteries, but the diastolic pressure *falls only slightly.*

Normal Blood Pressure Values.—An old wives' tale has it that the systolic pressure is normally 100 plus the age. This is not so, although there is a tendency for the systolic pressure to rise gradually with age. The normal systolic pressure in an adult can range from 90 to 150 mm., the diastolic level ranging from 60 to 90 mm. In young adults, the systolic should not exceed 140 mm. The difference between the systolic pressure and diastolic levels is known as the *pulse pressure.* It averages about half the diastolic level, and may normally range from 30 mm. when the systolic pressure is low, to 70 mm. when the systolic pressure climbs to its upper limit of normal.

Marked variations in blood pressure can occur in the course of a few minutes, due to excitement, apprehension, *etc.*, and the pressure taken when

a patient first enters the doctor's office may be 20 or more millimeters higher than the level a few minutes later. However, I am inclined to believe that the blood pressure reading should be done when the patient first enters the office and is apprehensive, because the higher reading so obtained may be an indication of potential hypertension, just as the cold pressor test and other procedures are

Eating, smoking, exercise may also raise the pressure, which may go as high as 200/110 after strenuous exercise. During sleep, the systolic pressure may fall 15 to 30 mm, and with prolonged rest in bed, there may be even a greater fall in blood pressure. On standing, the systolic pressure usually falls slightly, and the diastolic pressure rises slightly. On inspiration, the blood pressure may also fall a few millimeters.

Occasionally in normal persons, the diastolic pressure may be 0 mm. This is a transient phenomenon, and is associated with excitement and a normal or elevated diastolic pressure in the femoral artery, unlike aortic insufficiency, where a low diastolic pressure in the brachial artery is associated with a low femoral artery diastolic pressure.

Blood pressure readings can be taken from the right or left arm, but it should be remembered that the blood pressure reading from the right arm may normally be 10 mm higher than from the left, occasionally it is lower.

Femoral or Popliteal Artery Pressure.—Blood pressure in the femoral or popliteal artery is normally higher than in the brachial artery, and may equal or exceed 150/90 in the lying position, becoming still higher on standing because of the added hydrostatic pressure of the blood column. In taking blood pressure readings of the lower extremity, the cuff is placed around the mid-thigh. If it tends to slip, it can be held in place by wrapping a 3" roller bandage or an Ace bandage around it. Auscultation is done in the popliteal fossa. (The popliteal artery is a direct continuation of the femoral artery.) The patient either stands, or lies on his abdomen.

The high pressure in the femoral artery is due to the large caliber of the vessel and to the fact that the great circumference of the mid-thigh and the deep location of the femoral artery here, make it necessary to apply more pressure than exists in the artery to compress it.

Although the systolic blood pressure in the thigh may be 10 to 40 mm Hg higher than in the arm, the diastolic pressure is essentially the same in the thigh and arm.

If it is difficult to obtain the femoral blood pressure, the systolic pressure can be easily obtained at the ankle in the following way: with the patient lying down, the cuff is applied just above the ankle, with the bag on the anterior medial aspect of the leg, just above the ankle. The systolic pressure is then determined by palpating the dorsalis pedis artery.

Tests for Determining the Lability of Blood Pressure.—When marked fluctuations in blood pressure occur, or if transient hypertension is suspected from the history, the following tests can be done:

1. **The Cold Pressor Test.**—The subject is allowed to lie in a quiet room for about twenty minutes. Several blood pressure readings are taken until a basal level is approximated.

With the subject still lying, and with the blood pressure cuff on one arm, the opposite hand is immersed in ice water (4° C.) to a point just above the

wrist. With the hand still in the water, blood pressure readings are taken at the end of thirty and sixty seconds The highest of these two readings is taken as an index of the response. The hand is removed from the ice water as soon as the sixty second reading has been made, and readings are taken every two minutes until the blood pressure returns to its previous basal level.

The subject should have the nature of the test explained, to avoid apprehension, and he should not have taken sedative drugs for at least twenty-four hours prior to the test The temperature of the water should not vary more than 1° C.

Normally, the systolic pressure should rise not more than 20 mm., and the diastolic pressure not more than 15 mm. In addition, the maximal normal readings do not usually exceed 140/90.

2 **The Breath-Holding Test.**—With the patient sitting in a quiet room, the blood pressure is determined at five minute intervals, until a basal level is obtained This usually takes from twenty to forty-five minutes Then, at an observed moment of normal quiet expiration, the patient is told to compress both nostrils suddenly, and simultaneously close the mouth by compressing the lips The breath is held for twenty seconds, during which the systolic rise in pressure is determined. Following the rest period and a return to the basal level, the same test is repeated to determine the rise in diastolic pressure

The test causes stimulation of the vasomotor center because the carbon dioxide content of the blood is increased by the breath-holding, but normally the systolic and diastolic levels do not rise more than 22 mm

It should be pointed out that an abnormal response to either the cold pressor or the breath-holding test does not invariably mean that the subject will develop hypertension, nor does a normal response necessarily indicate that the subject will not develop hypertension. Furthermore, the subject may show varying responses at different times

Venous Blood Pressure.—This is described on page 107

The Radial Pulse.—Palpation of the radial pulse is a simple but integral part of the cardiac examination Palpation of both radial arteries should be done simultaneously. The tips of the fingers should be used, not the thumb Such examination can give the following information about:

1. **The Ventricular Rate.**—The resting pulse in adults varies from 60 to 100, but rates as low as 35 and as high as 120 can occur normally; and on exertion, the rate may speed to 200 or more Wide fluctuations in rate occur throughout the day, and during sleep the rate may slow markedly. (See also Chapter 18, page 319)

2 **The Ventricular Rhythm** —The heart may beat regularly and rhythmically, but respiratory variations are common, the rate increasing on inspiration, but slowing at the height of inspiration and during early expiration (sinus arrhythmia) (see page 320).

3 **Equality of the Pulses.**—Bilateral equality of the strength of the pulse is usually present, but moderate variations can occur, due to anatomical differences in the depth and location of the radial arteries, normal bilateral *variations in blood pressure, etc.* If there is marked inequality of the radial pulses, the brachial arteries should be palpated.

4. **The Pressure within the Radial Artery.**– An approximation of the systolic blood pressure can be obtained by noting the pressure necessary to obliterate the pulse wave With the tips of two fingers on the artery, pressure is applied with the proximal finger until the pulse is no longer felt by the distal finger

The effect of inspiration on the force of the pulse can also be noted. Normally no change may occur, or there may be a momentary, slight decrease in force.

5. **Volume Changes in the Radial Artery** The normal radial artery gives a moderate impact to the examining finger However, if the heart is beating rapidly, the pulse may develop a bounding quality.

6. **Physical Characteristics of the Radial Artery.** Palpation of the radial artery reveals it to be smooth, soft, and not tortuous

The Femoral Artery Pulse.– The femoral artery is normally strongly palpable in the groin, just below the inguinal ligament, mid-way between the anterior superior spine of the ilium and the symphysis pubis. Simultaneous palpation of the femoral and radial arteries is sometimes done. Normally the femoral pulse is palpable to the finger tips a moment earlier than the radial pulse

EXAMINATION OF THE NECK VESSELS

Neck Vessel Pulsations. On lying, a slight prominence of the external jugular vein may appear at the base of the neck, just above the clavicle, especially on the right side This should disappear on sitting or standing.

A pulsation of the jugular veins may also be seen. This appears as a series of two small waves separated by a deep trough with each heart beat. he waves correspond to the *a* and *v* waves of the jugular phlebogram, e 52 The *c* wave, recorded by the phlebogram, is usually not visible the naked eye.) The trough between the waves is more apparent than their crests and occurs simultaneously with the radial pulse. This is the reason that the normal jugular pulse has been called the *negative venous pulse* The presence of the systolic collapse of the jugular veins is very important especially in the differential diagnosis of cardiac arrhythmias because it indicates that sinus rhythm or one of its variants is present.

These venous pulsations should not be confused with arterial pulsations from the carotid or subclavian arteries, which also may be present. Venous pulsation can be differentiated from arterial pulsation by palpation. When the finger tips are placed over a venous pulsation in the neck, the pulse wave disappears under the touch. An arterial pulsation becomes stronger as pressure from the finger is applied, and is synchronous with the radial pulse. (However, an abnormal venous pulsation can also be synchronous with the radial pulse, page 149) In addition, the venous pulsations are diffuse, the arterial localized. Another point of difference is that the normal venous pulsations disappear higher in the neck, whereas the arterial pulsations are felt just as strongly.

Neck Vessel Sounds and Murmurs.—The following sounds and murmurs may be heard normally on auscultating the supraclavicular fossæ or the suprasternal notch:

1. **Heart Sounds.** The first and second heart sounds may be heard even in the neck, above the clavicles, especially on the right side. Occasionally in an obese person, the heart sounds are heard better in the neck than over the precordium.

2. **Arterial Sounds.**—Vascular sounds can also be heard. A soft systolic arterial whiff can be heard over the carotid artery if it is partially compressed by the stethoscope. (A similar sound can be heard over any large artery on compression. This is the origin of the sounds heard over the brachial artery when the blood pressure is taken.) This arterial sound may also be heard beneath the clavicles, at the junction of their middle and outer thirds. This is due to compression of the subclavian artery between the clavicle and the first rib. It can be accentuated by abducting the arm, which causes compression of the artery.

3. **Venous Hum.**—In addition to arterial sounds, a low-pitched, soft, continuous hum, accentuated during diastole, can be heard at the base of the neck, over the clavicles, especially on the right side. It is due to the rapid flow of blood through the jugular vein into the superior vena cava. Constriction of the vein may play a part in the production of this murmur, because it becomes accentuated when the head is turned to the opposite side.

This venous hum can be transmitted downward along the sternal border and may be mistaken for a cardiac murmur. It can be made to disappear by gentle pressure over the jugular vein, or by having the patient lie. It is accentuated on sitting and standing. It is very common in children.

Examination of the Carotid Sinus Reflex.—See page 288

EXAMINATION OF THE THORAX

General Examination.—It is important to observe the exposed thorax of the patient, paying special attention to:

1. **The Shape of the Thorax.**—The thorax is normally symmetrical, although slight prominence over the precordium may occur. Examination of the back should be routinely done to determine if kyphoscoliosis is present. The transverse diameter of the thorax is greater than the antero-posterior diameter, in an adult the ratio being about 2:1.

2. **Character of Respirations.**—The respiratory rate varies from 16 to 20 per minute in a normal adult. Breathing should be rhythmic and quiet, unless the patient is apprehensive, or becomes conscious of the examiner's interest in the respiration. For this reason, I distract the patient's attention by holding his wrist as if to take his pulse.

The respiratory excursion of the thorax is normally symmetrical. This can be determined by inspection, or palpation. A simple procedure to use is to place the palms of the hands on the lower ribs, thumbs on the costal angle, pointing to the xiphoid process. With inspiration, both thumbs should flare out equally.

Inspection and Palpation of the Chest Wall.—The following observations can be made:

The Apical Impulse.—The apical impulse should be studied by inspection and palpation. The apex of the heart may or may not be normally visible, but it is normally palpable, except in very obese people. Actually it is not

the apex of the heart which is palpable, but a region of the anterior wall of the ventricle, medial to the apex Palpation of the apical impulse is done by placing the finger tips in the fourth, fifth, or sixth intercostal space, as is necessary, to find the point of maximum impact

Palpation of the apical impulse is important because it is used to time pulsations, thrills, sounds, and murmurs elsewhere on the chest or body. *A pulsation, thrill, sound, or murmur which occurs simultaneously with the apical impulse is systolic in origin* If it occurs after the apical impulse is felt, it is diastolic (see also page 11) In addition, by palpating the apical

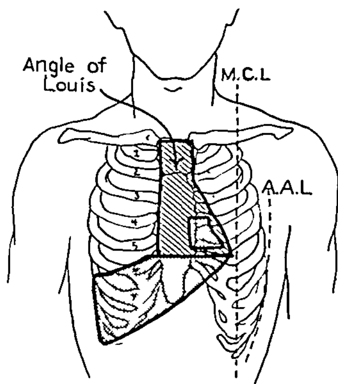


FIG 1 —The normal areas of cardiac dullness and flatness The flatness of the liver is also shown Striped area represents cardiac dullness Stippled area represents the area of cardiac flatness, and the flatness of the liver A A L, anterior axillary line, M C L, midclavicular line

impulse a rare case of dextrocardia may be discovered.

The normal apical impulse is located in the fifth intercostal space, within the left midclavicular line. The interspaces should be determined from the angle of Louis, the horizontal ridge which marks the junction of the manubrium and body of the sternum (Fig. 1) When the palpating finger feels this horizontal ridge and then glides downward and outward, it enters the second intercostal space In a woman, the apical impulse should be palpated beneath the breast, which should be elevated. The point of attachment of the lower margin of the breast to the pectoral muscles is at the fifth intercostal space.

The location of the apex can also be [illegible] Its distance may vary from 7 to 10 cm. [illegible] depending on the size and shape of the thorax. I [illegible] tance. The location of the apex should not be [illegible] nipple, the position of which can vary greatly.

The apical impulse lifts the palpating finger [illegible] thin and the heart is beating rapidly. The [illegible] can be covered by one finger If the apical impulse [illegible] pation, strong pressure by the palms against the [illegible] may make it palpable.

The location of the apical impulse can vary [illegible] respiration On expiration, and on lying [illegible] ward the left anterior axillary line. On [illegible] right side, the apical impulse shifts toward [illegible] of movement of the apex is not necessarily [illegible]

Other Chest Wall Pulsations.—These should [illegible] lightly on the chest wall over the second [illegible] adjacent portion of the sternum; over the [illegible] spaces near the sternum; and over the left [illegible]

The following pulsations may normally [illegible]

1. In thin-chested people, a slight systolic [illegible] third left intercostal space, near the sternum [illegible] monary artery

2 Lower down, along the left sternal border, [illegible] tion of the precordium may occur with each heart beat, [illegible] seen in the epigastrium It occurs because the [illegible] tends to recede from the chest wall

3 A localized systolic epigastric expansile [illegible] the abdominal aorta, may appear, especially if the [illegible] Differentiation of this pulsation from liver pulsation [illegible] 172.

4 In thin-chested people, especially children and [illegible] heart beating forcibly, a localized apical pulsation [illegible] tole It is coincident with the third heart sound, and [illegible] flow of blood into the ventricles during early diastole [illegible]

Percussion of the Heart —I don't routinely percuss the chest to deter- mine the size or outline of the heart, because [illegible] accurate However, at the bedside, percussion [illegible]

Method.—Before percussing the heart, I routinely [illegible] thorax, using fairly heavy blows of the flexed fingers [illegible] the back of the on the chest wall This is particularly valuable [illegible] directly tive of pleural effusion. [illegible]

In percussing the heart, the middle finger of the left hand is placed firmly against the chest, in an intercostal space, in a direction parallel to the [illegible] The middle finger of the right hand strikes it, just behind the nail, [illegible] quick, light, rebounding stroke, directed from the wrist. One should [illegible] not only where dullness and flatness begin, but also the sense of resistance that the underlying skin and tissues impart to the fingers. For example, over aerated lung, a resonant percussion note is associated with very [illegible]

sense of tactile resistance. As the heart is approached, the percussion note becomes dull, along with the tactile impression of resistance. This tactile impression enables one to percuss very accurately. Percussion is best done with the eyes closed or with the vision directed away from the chest, to rule out suggestion, for I have more than once seen an enthusiastic examiner map out the outline of the heart on the left chest in a patient with dextrocardia. The points where dullness appears can be marked on the skin, either with a special skin-marking pencil, or with ink, and the various points joined to form an outline of the heart. The normal outline of the heart is shown in figure 1.

The patient should be lying, because in this position, the most accurate outline of the heart can be obtained On sitting or standing, the cardiac silhouette becomes smaller, and a smaller area will be percussed Percussion will also give erroneous information in emphysematous patients, the hyperresonance of the lungs obscuring the cardiac outlines Similarly, accurate percussion may be impossible in a very obese person.

In performing percussion, I am usually more interested in determining where abnormal areas of dullness are located, rather than in making actual measurements of the size of the heart, determined by percussion

The following regions may be separately percussed.

1. Percussion of the first intercostal space, to the right and left of the sternum, to determine widening of the aorta (or mediastinum). Normally, dullness first appears when the sternal borders are reached

2 Percussion of the right third and fourth intercostal spaces determines enlargement of the right or left auricle or both Normally dullness occurs as the sternum is reached

3 Percussion of the left third intercostal space determines enlargement of the pulmonary artery Dullness normally occurs from 3.5 to 4.5 cm from the midsternal line. This is about half the distance of the apex to the midsternal line

4. Percussion of the left fifth intercostal space determines the outer border of the apex of the heart Dullness occurs from 7 to 10.5 cm. from the midsternal line This point is normally about 1.5 cm to the left of the point where the maximum apical impulse is palpated.

5 Percussion of the cardiohepatic angle.—The cardiohepatic angle is *obtained by joining the line drawn downward along the right border of* cardiac dullness, with the horizontal line drawn on the right lower chest, produced by the upper level of liver dullness. Normally this angle is a right angle (Fig 1).

The Area of Cardiac Flatness.—Most of the heart is covered by the lungs, so that percussion over the heart produces a moderately dull note. However, at the lower left border of the sternum, the heart is not covered by lung, and percussion produces a flat note over a triangular or irregular square area which extends from the sternum almost to the left midclavicular line, and begins as high as the fourth intercostal space (Fig. 1). The lower border of this flat area cannot be determined by percussion because it merges with the flatness of the liver. It is not necessary to outline this area routinely; its greatest value is in the diagnosis of pericardial effusion and enlargement of right and left auricles (page 157).

Auscultation of the Heart.—Auscultation of the heart represents neither the beginning nor the end of the cardiac examination Another point to remember is that the characteristics of the heart sounds are frequently more important than the presence or absence of murmurs.

Physical Characteristics of Sound.—Sound, murmurs, and other audible phenomena heard in any region of the body can be described in terms of (1) pitch and (2) intensity.

1. *Pitch.*—Pitch is determined by the number of vibrations of the sound per second. When the equilibrium of any elastic body is suddenly disturbed, it vibrates back and forth for a variable period of time. Thus, when a violin string is plucked, its vibrations can be seen, and a sound ensues. A low-pitched sound (like the G string sound of the violin) is associated with slow vibrations A high-pitched sound (like the violin E string sound) is associated with rapid vibrations.

The terms high-pitched and low-pitched, as used in cardiology are relative. This becomes obvious when one realizes that the human ear can distinguish sounds with 16 to 36000 vibrations per second. The first heart sound, which is comparatively low-pitched, has about 55 vibrations per second The second heart sound, which is relatively high-pitched, has about 62 vibrations per second

2. *Intensity of Sound.*—The intensity of a sound depends on the force of the vibrations. Thus, a G string plucked gently emits a soft note of G. When it is plucked forcibly, it emits a loud G note

Stethoscopes.—Two types of stethoscopes are in general use, the open bell type, and the diaphragm (Bowles) type. The diaphragm acts as a filter by decreasing the intensity of low-pitched sounds. This allows soft, high-pitched sounds to be heard more clearly. When the open bell stethoscope is applied to the chest, the skin acts as a natural diaphragm, and the harder the bell is pushed against the chest, the more taut the skin becomes, making the high-pitched sounds more distinct However, with the use of the Bowles stethoscope, pressure on the chest is not needed. For routine purposes I use this type stethoscope. One should not forget that the naked ear, placed on the chest wall, serves admirably as a stethoscope, and is particularly valuable in listening to high-pitched sounds and murmurs

The angle of the stethoscope ear tips should be adjusted to fit snugly in the external auditory canals, because if the ear tip openings are pressed against the walls of the canals, the heart sounds may become greatly muffled For this reason one should always test a new stethoscope by raising or lowering the ear piece to find the position that transmits the heart sounds best The tubing should be as short as possible, because a long tubing absorbs sounds and decreases their intensity. An adequate length is 10 inches

The stethoscope efficiency can also be increased by using a tubing with a narrow bore of $\frac{1}{8}$ inch, rather than the conventional $\frac{3}{16}$ inch bore.

Another simple but valuable procedure in auscultation is to have the patient hold his breath when you are concentrating on particular sounds or murmurs. This eliminates the interference of breath sounds.

The Cardiac Cycle.—The heart sounds are produced by vibrations of the valves and possibly the muscles of the heart. This can be best explained in terms of the cardiac cycle:

sense of tactile resistance. As the heart is approached, the percussion note becomes dull, along with the tactile impression of resistance. This tactile impression enables one to percuss very accurately. Percussion is best done with the eyes closed or with the vision directed away from the chest, to rule out suggestion, for I have more than once seen an enthusiastic examiner map out the outline of the heart on the left chest in a patient with dextrocardia. The points where dullness appears can be marked on the skin, either with a special skin-marking pencil, or with ink, and the various points joined to form an outline of the heart The normal outline of the heart is shown in figure I

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aortic area In adult life, the intensity at both locations is equal. In old age, the aortic second sound (A2) is louder than the pulmonary second sound (P2 In obese people, both heart sounds may be very faint. The phonetic equivalent of the two heart sounds is *lub dub*. If the three heart sounds are present, the phonetic equivalent is *lub dub da*.

The third sound is inconstant and is not ordinarily heard in adults, but appears in children and young adults. When present, it can be heard best in the fourth left intercostal space, between the sternum and the apex of the heart It can be elicited by exercise, lying on the left side, or increasing the venous return by pressure on the abdomen or raising the legs.

There is a short pause, during systole, between the first and second sounds, and a long pause, during diastole, between the second and first sounds When a third sound is present, it is heard fairly early in diastole, about 0 12 to 0 18 second after the second sound.

The Valve Areas.—The valve areas described above do not represent the anatomical position of the valves, but merely indicate points where sounds, thrills, or murmurs originating in the valves are frequently heard or felt well The actual anatomical locations of the valves are shown in figure 2.

Auscultation of the heart should not be confined to the valve areas I usually auscultate over the following regions:

1. The right supraclavicular fossa. Venous and arterial sounds, and murmurs transmitted from the base of the heart are heard well here.
2. The suprasternal notch. Aortic murmurs are sometimes heard very well here
3. The aortic area.
4. The pulmonary area.
5. The third left intercostal space, where aortic murmurs are often heard best
6. Downward along the left sternal border and toward the apex
7. The apex, and then outward to the left anterior axillary line.

Timing of the Heart Sounds.—The heart sounds should always be timed in relation to the apical impulse or the carotid artery pulsation. The first sound occurs simultaneously with the apical impulse or carotid artery pulse. The second and third sounds occur after the apical impulse is felt. The radial artery pulse can also be used to time heart sounds and other cardiac phenomena, but one should remember that the time of onset of the pulse in the radial artery occurs slightly later than in the carotid artery, just as the carotid pulse occurs slightly later than the apical impulse

Splitting or Reduplication of the Heart Sounds—Splitting or reduplication of the first and second sounds may occur normally.

A split first sound can be recognized by the phonetic equivalent *l-lub dub* It is best heard at the apex, and on standing, especially in thin-chested people. It may be produced normally in several ways: the auricular component of the first heart sound may be heard separately; asynchronism of the right and left ventricles may occur, vibrations may be set up by the act of the heart against the chest wall (See also page 55)

A split second sound can be recognized by the phonetic equivalent *lub dl*. It is best heard at the base, especially on lying and during expira- It is due to asynchronous closure of the aortic and pulmonary valves. page 55)

Splitting of the heart sounds should always be considered normal unless examination reveals abnormal conditions such as bundle branch block or pulmonary hypertension, which can produce splitting abnormally.

Cardiac Murmurs. A murmur may be defined as an extraneous sound, of longer duration than the regular heart sounds, produced by vibrations of the ventricular walls, the valves, or the walls of the blood vessels.

Classification of Murmurs - Innumerable classifications of murmurs have been proposed. For present purposes, murmurs can be classified as *normal*

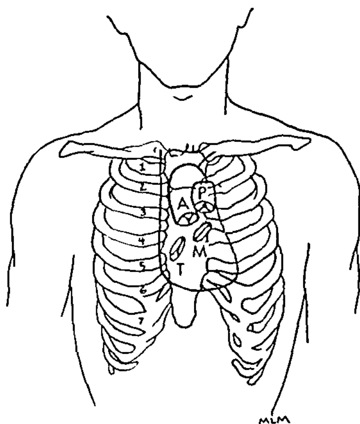


FIG 2 — Diagram showing the anatomical projections of the valves on the chest wall These should not be confused with the locations of the so-called valve areas (p 41) A, aortic valve, M, mitral valve, P, pulmonary valve; T, tricuspid valve.

or *abnormal* Normal murmurs have also been called functional, haemic, physiologic, accidental, innocent, *etc*

Genesis of Murmurs.—Murmurs (normal or abnormal) can be produced in three ways.

1. *Murmurs by Collision.*—Such murmurs are produced when the column of blood strikes the wall of the heart or of a large blood vessel more or less perpendicularly, causing it to vibrate. The normal systolic murmur at the apex may be produced in such a way if blood regurgitates from the left ventricle and strikes the wall of the left auricle. The abnormal murmur of mitral insufficiency is also produced in this way.

2. *Murmurs Resulting from Free Currents.*—When fluid or blood flows through a tube with smooth, even walls, no murmur appears until the velocity of the flow increases beyond a critical rate. The murmur in such a case is due to eddies produced in the blood stream and transmitted to the vessel wall. A decreased viscosity of the blood, such as occurs in anemia favors the production of this type murmur An increased viscosity of the blood, such as occurs in polycythemia, tends to prevent the appearance of this form of murmur.

Irregularities of the vessel wall predispose to eddy formation. Thus, in the heart, with its irregular walls and numerous membranes and tendinous structures, very favorable conditions exist normally for the production of murmurs. The reason they are not heard ordinarily is that the velocity of the blood stream is too low. However, with the forceful beating of the heart in children and young adults, and with the tachycardia of exercise, fever, anemia, hyperthyroidism, *etc*, systolic murmurs appear very frequently at the apex and pulmonary area in this way

3. *Murmurs Produced by Strings.*—Murmurs can also be produced by free-floating chordæ tendineæ, or bands in the ventricular cavity, which are set in vibration by eddies around them In such cases, harsh and sometimes musical murmurs appear. These murmurs are not normal.

Method of Describing Murmurs.—Murmurs are usually described according to the following characteristics·

1. *Time of Appearance* —Murmurs may be systolic or diastolic. The presystolic murmur is a variety of the diastolic A general rule that I have found useful is to consider a systolic murmur normal until proven otherwise. Diastolic murmurs, on the other hand, are almost always abnormal. (Rarely the diastolic component of a venous hum may be transmitted downward over the heart) The timing of murmurs is described on page 36.

2. *Location of Maximum Intensity* —Murmurs heard best at the apex are often the result of mitral involvement, but may be transmitted from the aortic valve and elsewhere. Murmurs heard best at the second interspace to the right of the sternum (the aortic area) frequently arise from the aortic valve, but may be transmitted from the pulmonary valve or the neck vessels or elsewhere Murmurs heard best at the second or third interspace to the left of the sternum (the pulmonary area) may arise in the pulmonary valve or the aortic valve, or elsewhere. Murmurs heard best at the xiphoid process or at the fourth and fifth intercostal space, to the right of the sternum (the tricuspid area) may arise from the tricuspid valve, or the mitral valve, or elsewhere. Normal systolic murmurs are common at the apex and pulmonary area, rare at the aortic area.

3 *Pitch* —Murmurs can be described as high- or low-pitched. However, pitch cannot be used to differentiate normal from abnormal murmurs.

4. *Intensity.*—Murmurs can be classified into six grades: grade 1, the faintest murmur that can be heard on careful auscultation, grade 2, slight, grade 3, moderate; grade 4, loud; grade 5, very loud; grade 6, a murmur that can be heard with the naked ear at a distance from the patient.

5 *Duration* —A murmur may be short, or may occupy the entire period of systole or diastole. Normal murmurs are usually short in duration, and do not mask or replace the first or the second sound

6. *Transmission* - Murmurs that arise at the base of the heart are often transmitted upward to the neck, and downward along the left sternal border, and to the apex. Murmurs that arise at the apex, however, are not transmitted as high as the base, but rather toward the axilla. This is the reason that, in auscultating the heart, I first listen over the neck, then over the base of the heart, along the left sternal border, and finally over the apex. However, the louder a murmur, the more widely it is transmitted.

7. *The Effect of Posture, Exercise, Respiration* - The effect of changes in posture, exercise, or respiration on a murmur, or the constancy or inconstancy of a murmur cannot be used as a guide in determining whether the murmur is normal or abnormal. However, these procedures are helpful in making murmurs audible or in increasing their intensity. This is discussed in more detail on pages 161 through 169.

8. *Presence of Thrills* —See page 155

9. *Confirmatory Signs of Heart Disease.*—When a systolic apical or pulmonary murmur is present, the absence of physical or laboratory signs of enlargement of the heart or of heart failure suggests that the murmur is normal. However, I should like to emphasize again that a murmur does not necessarily indicate a damaged heart, nor does the absence of a murmur indicate that the heart is normal. The prominent pulmonary systolic murmur of normal children, and the absence of murmurs in acute and fatal myocardial infarction is ample proof of this.

Normal Murmurs.—The following are some of the more common normal murmurs

1. *The Pulmonary Systolic Murmur* —This is a soft, low-pitched, systolic murmur, which begins early in systole but does not mask or replace the first heart sound. It is heard best in the third intercostal space, to the left of the sternum, and is transmitted along the left sternal border toward the apex. It may be associated with a split second sound. It is due to the rush of blood into the distended pulmonary artery, and is loudest on lying and during expiration, possibly because under these conditions the pulmonary artery is nearest the surface. It is the most common of normal murmurs. Rarely a soft, low-pitched, systolic murmur is heard at the aortic area. This may be transmitted from the neck vessels. An interesting explanation for the pulmonary systolic murmur has recently been proposed, namely that the pulmonary valve orifice is easily stretched when the artery dilates, but the free edges of the valve cusps are very resistant to stretching. Therefore, the free edges of the valves make three cords across the vessel during systole instead of lying closely to the vessel wall. This process, trigonoidation, produces a relative pulmonary stenosis.

2. *The Apical Systolic Murmur* —Differentiation of a normal from an abnormal systolic murmur at the apex is a difficult problem, and there has been much discussion and little agreement as to what constitutes a normal or an abnormal apical systolic murmur. The following description of the normal apical systolic murmur therefore reflects my own experience:

It is heard best at the apex as a soft, blowing, low-pitched murmur, which, like the pulmonary systolic murmur, begins early in systole and does not replace the first heart sound. It is more or less localized, is not transmitted toward the axilla, and is not associated with signs of cardiac enlarge-

ment. The cause of this murmur is unknown One explanation is that it is due to incomplete closure of the mitral valve during systole, with functional mitral regurgitation Since it frequently appears with excitement, exercise, fever, and many other conditions which produce a tachycardia and an increased blood flow through the heart, it is possible that eddies produced by the rapid passage of blood through the heart cause the murmur.

I have found that many so-called apical murmurs are not apical, but are transmitted from the pulmonary artery or the neck vessels This occurs most frequently in normal persons with a long, thin heart, where the apex lies well within the left midclavicular line.

A normal apical systolic murmur will not show systolic expansile pulsation of the left auricle on fluoroscopic examination. An abnormal systolic murmur, due to mitral insufficiency may show this (page 190).

Extraneous Normal Heart Sounds.—The following extraneous heart sounds may be heard normally:

1. *Cardio-Respiratory Murmurs* —These are interrupted breath sounds produced by the mechanica movement of the heart upon the surrounding lung tissues, causing air to be sucked in or out of the alveolar spaces. They are heard as a series of two or three soft puffs with each heart beat. They are usually systolic in time, occasionally diastolic They may be heard at the apex, over any region of the precordium, even in the back, especially at the angle of the left scapula They sound very close to the ear, are not transmitted in any characteristic direction, are increased by inspiration, and usually disappear when the breath is held. They may also disappear on lying.

2 *The Mid-Systolic Click.*—This is a sharp, snapping or clicking sound, or a succession of two or three clicks heard midway between the first and second sounds, within the apex. It is probably due to the pressure of the contracting heart on an emphysematous bleb.

3. *The Mid-Systolic Gallop* —This is a cadence of three sounds produced by an additional sound which occurs midway between the first and second heart sounds It is heard best at the apex, and disappears at the base. It may be identical with the mid-systolic click A systolic gallop has also been described over the aortic area, but this is rare in normal people except during febrile states

4 *The Substernal Crunch* (*Xiphosternal Crunch*) —This is heard as a short, harsh, crunching, scratching or scraping noise just to the left and above the xiphoid cartilage It occurs in systole and diastole, seems close to the ear, and is increased in intensity when the patient leans forward or to the left Some degree of funnel chest is often present. The cause of the crunch is unknown It may be due to movement of the articulation of the seventh costal cartilage with the sternum and xiphoid process.

Other Extraneous Sounds —Contraction of the pectoral muscles may produce a low-pitched roaring and drumming, or a dull, short, rumbling sound Similarly, the crepitation of hair under the stethoscope bell or diaphragm, or rubbing together of the stethoscope tubing should not be misinterpreted as abnormal heart sounds. Rarely, spasmodic contractions of the diaphragm (diaphragmatic flutter) produce sounds audible over the precordium, which superficially resemble auricular fibrillation.

EXAMINATION OF THE ABDOMEN

The cardiologist is principally interested in the abdomen to determine enlargement of the liver, splenomegaly, and the presence of ascites.

The Liver.—The right lower edge of the liver can be determined by percussion or palpation. Percussion is frequently preferable, because when the liver is very large, its edge may extend below the umbilicus and can be missed by superficial palpation. Percussion over the liver yields a flat note. Normally the percussion note over the abdomen is tympanitic up to the costal margin

On palpation, the right lower edge of the liver frequently is felt just beneath the costal margin. If it is not palpable, the fingers of the hand can be hooked under the ribs and the patient told to breathe deeply The liver descends 1 or 2 inches with inspiration and its edge can then be felt, smooth, soft, and not tender. Palpation should be done laterally near the right anterior axillary line, because near the center of the abdomen, the transverse tendinous intersections of the abdominal recti muscles can be mistaken for liver edge.

The right upper edge of the liver can be determined by percussion of the thorax in the right midclavicular line Normally liver flatness begins as high as the fifth intercostal space In the right midaxillary line, liver flatness begins at the seventh intercostal space (Fig 1, page 36). Posteriorly, below the angles of the scapulæ, liver flatness begins at the level of the ninth or tenth thoracic vertebra (the angle of the scapula is at the level of the seventh thoracic vertebra).

The Spleen.—The spleen normally is not palpable. Palpation for the spleen can be done by having the patient lie on the right side, while the examiner stands behind him, and hooks his fingers over the ribs in the left hypochondrium The patient then takes a deep breath. In this way, a spleen slightly enlarged may be felt at the end of a deep inspiration.

Another method of palpating for the spleen is to have the patient lie on his back, knees drawn up, the abdomen relaxed. The examiner stands to the right of the patient, facing him. One hand is placed posteriorly over the splenic region and presses anteriorly. The other hand dips beneath the left costal margin The patient is then asked to take a deep breath. In this way also, the edge of a slightly enlarged spleen may be felt at the end of inspiration

Ascites.—The diagnosis of ascites is described on page 173.

TAKING THE TEMPERATURE

The so-called normal body temperature of a healthy person has been stated categorically to be 98 6° F. (37.0° C) Another clinically accepted truism is that the rectal temperature is 1° F. higher than the oral, or approximately 99 6° F (37.6° C.) However, these values are merely approximations and can be highly misleading especially in cases where rheumatic fever or subacute bacterial endocarditis is suspected.

Recent studies by the Council on Physical Medicine of the American Medical Association have shown that the normal rectal temperature may

exceed 100° F., and that the difference between rectal and oral temperatures may exceed 2° F or may be less than ½° F In addition, the temperature of a person during the course of the day can vary 1° F, and probably more

Whenever possible, rectal rather than oral temperature should be taken because it is not rare to find an oral temperature of 99.0° F to 99.6° F in the presence of a normal rectal temperature.

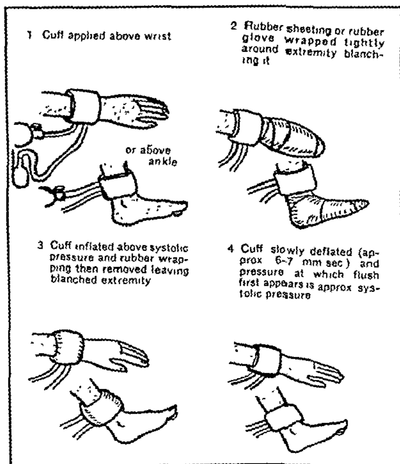


Fig 3 —Method of taking systolic blood pressure in an infant (after Goldring and Wohltmann)

SOME PHYSICAL FINDINGS IN NORMAL INFANTS AND YOUNG CHILDREN

Blood Pressure.—In early infancy the systolic pressure averages from 60 to 90 mm. mercury, gradually rising in childhood so that at the age of twelve years it is about 105 mm. By late adolescence the systolic pressure is 120 mm. Diastolic pressure is difficult to obtain in infants and young children. It averages about 40 to 70 mm with a pulse pressure of 20 to 30 mm

Blood Pressure Determinations in Infants and Young Children.—If a cuff which is too wide is used on an infant or young child, a reading 20 to 25 mm. Hg too low may be obtained. Cuffs having the following widths therefore are recommended by the American Heart Association: for children under eight years, 8 or 9 cm.; under four years, 5 or 6 cm.; under one year, 2.5 cm. or less.

The following flush method has been described to obtain the systolic blood pressure in the infant by inspection. a 2.5 cm. cuff is placed around the ankle or wrist in the usual manner and a piece of rubber sheeting or old rubber glove is wrapped snugly around the foot or hand, starting distally, so that the blood is pressed from the extremity. The cuff is then inflated to a pressure slightly above the suspected systolic pressure, the rubber bandage is then removed from the blanched extremity and the pressure is slowly reduced in the cuff, not faster than 6 to 7 mm. Hg per second. The approximate systolic pressure is the reading at which blood re-enters the foot or hand, causing a sudden flush (Fig. 3).

The Pulse.—Marked sinus arrhythmia is common. Frequently the finger feels a soft pulsation immediately following the main pulse wave (dicrotic pulse) with each heart beat. This is merely an exaggeration of the normal radial pulsations which appear when recorded (page 54).

The heart rate varies greatly. Average rates are as follows: at birth, 110 to 150, two years, 82 to 125, four years, 75 to 115; six years, 65 to 105; over six years, 60 to 100.

The Thorax.—In infants, the thorax tends to be cylindrical and the ratio between the transverse and antero-posterior diameters of the thorax is 1:1, unlike the 2:1 ratio in adults. In other words, the antero-posterior diameter of an infant or young child is relatively larger than an adult's.

Respiratory activity in infants and children is quite shallow and irregular, especially during sleep. The respiratory rate may be quite rapid: at birth 44 per minute, one to two months, 24 to 36, two to five months, 20 to 3? and after that until the tenth year, 20 to 28.

The Heart.—The apex is normally found in the fourth left interco[...] space, even 1 cm. outside the midclavicular line. This relation may per[...] until the thirteenth year. Dullness at the apex also extends beyond [...] left midclavicular line. At the base, dullness may extend beyond the s[...]num to the left of the first and second intercostal spaces, and may ext[...] to the right of the sternum, if the thymus is large. However, the third [...] fourth intercostal spaces, to the right of the sternum, are normally reson[...] With each heart beat, a diffuse, undulatory movement of the left side of [...] chest may occur.

At birth, the heart sounds have a tic-tac rhythm. This gradually dis[...]pears, but the first and second sounds remain equal in amplitude until [...] end of the second year when the first heart sound develops the musc[...] tone heard in adults. The pulmonary second sound is accentuated.

A loud systolic murmur may be heard shortly after birth. This is [...]sibly due to the flow of blood through the ductus arteriosus. In a wee[...] so, the murmur disappears. However, systolic apical and pulmonary m[...]murs are common in infancy and childhood. The venous hum is rar[...] infants but common in children.

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Chapter 2

RECORDING AND TIMING OF HEART SOUNDS, MURMURS, AND PULSATIONS OF THE HEART AND BLOOD VESSELS

INTRODUCTION

HEART sounds and murmurs can be studied not only by the usual method of auscultation but they can be electrically recorded. A tracing or record so obtained is known as a phonocardiogram or stethogram. However, just as it is necessary to time audible heart sounds and murmurs by means of the apical impulse or by means of pulsations of the carotid or radial artery, the recorded sounds must also be timed. This can be accomplished by recording the phonocardiogram simultaneously with an electrocardiogram, *or with the pulsations produced by the impact of the apex against the chest* wall (apex cardiogram), or with the pulsations produced by the propulsion of blood into the carotid, radial or any large artery (arteriogram), or with the pulsations produced in the internal jugular or any other vein (phlebogram). Tracings so obtained are chiefly of value in studying the physiology of the cardiac cycle and in identifying obscure sounds and murmurs. They are not necessary for routine purposes. For accuracy in analysis, the camera speed should be set at 75 mm. per second.

THE RECORDING APPARATUS

The instrument used in recording heart sounds and vessel pulsations consists essentially of a microphone, an amplifying system, and a recording galvanometer. The microphone used for this purpose is of the piezoelectric crystal type, which is able to convert vibrations set up by sound waves and pulsations into electrical currents which are amplified and recorded.

Three types of microphones are in current use:

1. **The Linear Microphone.**—This registers the sound vibrations as they exist on the surface of the chest and body. This microphone is used chiefly for recording pulse tracings, because when very low frequency pulsations are registered, the higher pitched heart sounds are not reproduced.

2. **The Logarithmic (Human Audiographic) Microphone.**—This registers the sounds as they are heard with the stethoscope by a competent observer. Sounds which are ordinarily inaudible will therefore not be recorded.

3. **The Stethoscopic Microphone.**—This registers sound vibrations as they are transmitted by an average acoustic stethoscope. This microphone records sounds which would be heard if the ear could hear all the sounds transmitted to it by the stethoscope. Thus the stethoscopic microphone records sounds which are not normally audible.

Both the logarithmic and stethoscopic microphones are used in recording heart sounds and murmurs. The logarithmic microphone is good for high-pitched sounds because it attenuates and suppresses low-pitched sounds. The stethoscopic microphone is good for routine purposes and for recording low-pitched sounds

PULSE TRACINGS

Briefly, the characteristics of the more common sound and pulse tracings, and their relations to the cardiac cycle are as follows

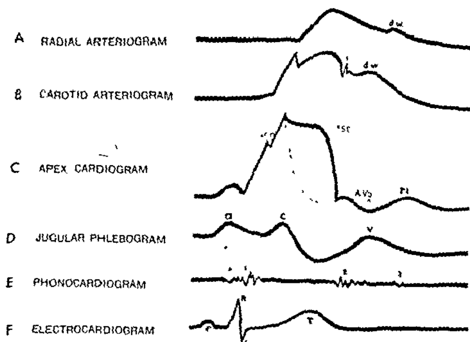


FIG 4 —Diagram showing the relations between pulse tracings, heart sounds and the electrocardiogram *AVo*, a-v valves open, d w, dicrotic wave; *i*, incisura, *ri*, wave of rapid inflow, *SC*, semilunar valves close, *SO*, semilunar valves open 1, 2, 3, 4, first, second, third and fourth (auricular) heart sounds See text for details

The Jugular Phlebogram (*Fig* 4, *D*).—The internal jugular vein lies in direct continuation with the right auricle and superior vena cava, so that pressure changes in the right auricle can be excellently recorded over the jugular vein Tracings are best obtained over the right jugular bulb, which lies at the base of the neck under the sterno-mastoid muscle Three pulsations, called the *a*, *c*, and *v* waves, normally are recorded.

The a Wave.—This is produced by auricular systole Its position is determined by the fact that it occurs about 0.2 second before the *c* wave.

The c Wave—The upstroke of the *c* wave begins simultaneously with the upstroke of the carotid arteriogram, and 0.1 second earlier than the up-

stroke of the radial arteriogram. The *c* wave occurs during ventricular systole while the first heart sound is being recorded, and is due to pulsations transmitted from the carotid artery and the aorta, and possibly from systolic pulsations transmitted from the right ventricle through the right auricle and superior vena cava.

The v Wave.—After the *c* wave, a prominent depression appears (the systolic collapse or the *x* wave). This is due to the downward movement of the tricuspid valve produced by the contracting right ventricle, thus decreasing the pressure within the right auricle. The *v* wave follows this depression It is due to the gradual filling of the right auricle while the tricuspid valve is closed. The summit of the *v* wave marks the approximate beginning of diastole, and the downstroke of the *v* is due to the opening of the tricuspid valve, causing the right auricular pressure to fall as blood flows into the ventricles. The summit of the *v* wave occurs about 0 11 second after the beginning of the second heart sound. The *v* wave can usually be identified from the shape of the jugular tracing alone, because it is usually preceded by a very deep depression A diastolic collapse (the *y* wave) then occurs An inconstant wave, called *h* or *b* occurring during the phase of rapid ventricular filling may also follow the *v* wave.

The Apex Cardiogram (Fig. 4, *C*).—This is produced by the impact of the heart on the chest wall With auricular systole, a small round deflection may appear. This is followed by a large upstroke due to ventricular systole This begins a fraction of a second after the onset of the first heart sound, and while the *R* wave of the electrocardiogram is being inscribed This upward deflection is divided into two portions by a notch which marks the opening of the semilunar valves This point is synchronous with the beginning of the rise of the carotid arteriogram.

A systolic plateau follows, and the deflection falls abruptly with the beginning of diastole and the closure of the semilunar valves A small after-deflection then occurs This is followed by a depression, and then by a final deflection, *ri*, which occurs simultaneously with the third heart sound and marks the rapid inflow of blood into the ventricles when the *a–v* valves open.

The apex cardiogram may show a deep systolic depression, if the microphone is not placed directly over the apex. (Fig 4, *C*, dotted line). This is due to the fact that part of the precordium sinks in during systole. This is especially noted over the right ventricle

The apex cardiogram can be used to time events in diastole, if it is difficult to obtain a jugular phlebogram, because its final *ri* wave occurs simultaneously with the third heart sound

The Carotid Arteriogram (Fig 4, *B*) —Small preliminary oscillations may occur before systole These are due to auricular contraction A sharp upstroke (percussion wave) occurs as blood is propelled into the aorta This upstroke is simultaneous with the upstroke of the jugular *c* wave Midway on it, a slurring or small notch may occur, the anacrotic depression.

Immediately after the peak of the upstroke, a small, momentary depression may occur, due to overshooting The deflection then remains up during systole (tidal wave) and falls abruptly with the closure of the aortic valve, producing a marked dicrotic notch or incisura, *i* which is followed by

small after-vibrations, and a gentle upstroke, the dicrotic wave, *dw*, which is due to vibrations set up by the elastic recoil of the aorta after the aortic valve closes.

The Radial Arteriogram (Fig. 4, *A*).—The upstroke of the radial arteriogram occurs 0.1 second after the upstroke of the carotid arteriogram because it takes the pulse wave that long to travel from the carotid to the radial artery. The upstroke is more gradual than the carotid, the incisura disappears and is replaced by a rounded depression and the dicrotic wave.

The Femoral Arteriogram.—This is similar to the radial arteriogram but it normally begins earlier than the radial and its peak occurs slightly earlier When compared to the carotid arteriogram, it begins slightly later and its peak occurs after the peak of the carotid arteriogram but before the incisura

Other Pulse Tracings.—Normally, liver pulsations are not palpable, but they can be recorded (hepatogram) The hepatogram resembles the jugular phlebogram, but the *c* wave is missing. Pulse tracings can also be taken from the esophagus (esophagocardiogram) and from the upper respiratory tract (internal pneumocardiogram). Tracings so recorded are very complex and have little clinical value

THE HEART SOUNDS

The Auricular Sound.—Contraction of the auricles frequently produces one or two small vibrations which begin at or after the peak of the *P* wave of the electrocardiogram The time relations between the auricular sound and the *P* wave are inconstant, but the auricular sound vibrations can be seen before the beginning of the *QRS* complex (Fig 4, *E*). They will also be found to occur after the rise of the jugular *a* wave, and before the upstroke of the carotid arteriogram

The auricular sound may be separated from the first heart sound, or may merge with it. However the auricular sound is usually not audible as a separate sound Occasionally it is heard and interpreted as splitting of the first heart sound The auricular sound is sometimes called the fourth heart sound.

The First Heart Sound (Fig. 4, *E*).—The first heart sound can be timed with the electrocardiogram because it begins a fraction of a second after the onset of the *QRS* complex (Therefore, all vibrations which precede the beginning of the *QRS* complex do not originate in the ventricles) It precedes the apex cardiogram by about 0 01 second

Phonocardiographic analysis of the first heart sound shows four components:

First Component.—This may be produced by residual auricular vibrations. One or two slow vibrations occur simultaneously with the beginning of the *QRS* complex.

Second Component.—This is produced by the closure of the mitral and tricuspid valves The vibrations have a higher frequency and greater amplitude than those of the first component. This component starts after the peak of *R* in the electrocardiogram, and ends before the rise of the *c* wave of the jugular pulse tracing. The first portion of the ascending limb of the apex cardiogram occurs simultaneously with it

Third Component.—This is produced by the opening of the aortic and pulmonary valves. This component may be slightly separated from the second component. It occurs with the rise of the jugular *c* wave, and the rise of the carotid arteriogram. The second portion of the ascending limb of the apex cardiogram occurs simultaneously with it

Fourth Component.—This consists of small, low frequency vibrations which occur immediately after the third component. It is due to the acceleration of blood in the large arteries after the aortic and pulmonary valves open.

The vibrations of the first sound should not extend beyond the peak of the *c* wave of the jugular pulse tracing, or beyond the peak of the apex cardiogram. If this occurs, it is indicative of a systolic murmur.

Audible splitting of the first heart sound occurs if the separation between the second and third components is pronounced Also, splitting may occur if the auricular sound is close to the first component of the first heart sound. Such splitting is normal (Splitting of the first sound can occur pathologically in cases of bundle branch block In such cases, phonocardiographic analysis shows that there are more than four components to the first heart sound, due to the marked ventricular asynchronism.)

The Second Heart Sound (Fig 4, *E*).—This is best timed with the carotid arteriogram, because the second sound begins almost simultaneously with the incisura of the arteriogram. Also the beginning of the second sound precedes the summit of the jugular *v* wave by a constant interval of 0.11 second The relation of the second sound to the electrocardiogram is variable. It usually begins slightly after the end of the *T* wave, but may precede the *T*.

Four components also have been described for the second heart sound:

First Component.—This consists of one or two small vibrations, which occur at the beginning of ventricular diastole.

Second Component.—This consists of several high amplitude vibrations caused by the closure of the aortic and pulmonary valves. It occurs during the ascending limb of the jugular *v* wave, and it is coincidental with the dicrotic notch of the carotid arteriogram. At this moment, the apex cardiogram shows a small upward wave, immediately after its steep decline.

Third Component —This is due to vibrations of the blood column after the closure of the semilunar valves. These vibrations are small in amplitude

Fourth Component.—This is due to opening of the mitral and tricuspid valves. It occurs simultaneously with the peak of the jugular *v* wave, and at the lowest point of the apex cardiogram before its wave of rapid inflow, *ri*.

A logarithmic microphone almost always totally obliterates the first, third, and fourth components of the second heart sound, whereas a stethoscopic microphone may show all four components Thus, in a logarithmic phonocardiogram, and to the listening ear, the second sound appears shorter than the first, whereas it has almost the same duration

Splitting of the second sound may occur normally as a result of asynchronous closure of the aortic and pulmonary valves. If this occurs, the third component of the second heart sound becomes longer, but the third

component still ends before the a-v valves open, and therefore before the peak of the jugular v wave This differentiates a split second sound from the opening snap of the mitral valve (see page 159)

The Third Heart Sound (Fig 4, E) - This may or may not be recorded. When present it is composed of one or two slow vibrations of small amplitude It can be timed because it occurs on the descending limb of the jugular v wave It also occurs simultaneously with the final ri deflection of the apex cardiogram

MURMURS

Murmurs (normal or abnormal) when present, will also be recorded as very rapid vibrations of large or small amplitude It is interesting to note that phonocardiographic records of the mitral area (the apex) show the presence of a systolic murmur in as much as 80 per cent or more of normal children, in spite of the fact that a systolic murmur is not audible. In the phonocardiogram a murmur can be identified as a series of abnormal waves of more than three vibrations Murmurs can also be described in terms of frequency, a high frequency murmur having more than 130 cycles per second, a low frequency murmur, less

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Chapter 3

X-RAY EXAMINATION OF THE HEART

By means of x-ray examination, the size, shape, and position of the heart and great vessels, as well as the characteristics of their pulsations, can be observed. The usual methods of x-ray examinations are fluoroscopy, orthodiascopy, teleoradiography, and angiocardiography For routine purposes, I prefer fluoroscopy.

FLUOROSCOPY

Fluoroscopy is a direct examination of the patient, who is placed between the x-ray tube and the fluorescent screen. Since the distance of the tube target and the screen is only 26 inches, the cardiac shadow on the screen appears larger than it really is The reason for this is that when electrons strike the tube target, the emitted x-rays diverge greatly, in addition to passing centrally out (Fig. 5, A). However, fluoroscopy is particularly valuable in studying the contours of the heart, the size of individual chambers, and abnormal pulsations, as well as the lung fields, which should also be routinely studied in every cardiac fluoroscopic examination

General Suggestions.—For fluoroscopy, a fine focus x-ray tube, and a fine grain fluorescent screen, such as the Patterson Type B, give best results The control dials should be set at a 5 inch gap (65 kv.) and 5 ma. current. For children, 4 ma is usually sufficient The fluoroscopy room should be completely dark, and one should not begin the examination until the eyes are well accommodated to the darkness This may take from ten to twenty minutes Protective gloves and apron should always be worn, and the shutters of the fluoroscope should always be slightly visible on the screen. This prevents the examiner from receiving excess stray radiation Also, by keeping the screen illuminated intermittently, the duration of exposure to x-rays is reduced and the tube is prevented from overheating

In order to keep exposure at a minimum, the physician should do fluoroscopy for not more than three to five hours a week, and should try to use 3 ma rather than 5 ma. The patient should not be exposed for more than five minutes at an examination

For studying fine detail, the shutters can be closed until an opening of a few square inches remains. In addition, visual acuity in the dark is improved by focusing the eyes just to one side of the area being studied, rather than looking directly at it. The patient should not have more than five minutes exposure at any one examination. The patient is usually fluoroscoped in the following three standard positions:

A. **The Posterior-Anterior (P-A) Position** (Fig. 6).—The patient stands, facing the screen.

The Right Border of the Heart—From above downward, three contours may be seen

1. The superior vena cava which runs vertically and close to the spine. The right innominate vein and sometimes the innominate artery may also occupy part of this shadow.

2. Below this, the convex right margin of the ascending aorta is superimposed on the shadow of the superior vena cava, and may reach the right border of the heart

3. Below this, the convex border of the right auricle extends to the diaphragm. On deep inspiration, a small triangular shadow may appear between the lower border of the right auricle and the diaphragm. This is the inferior vena cava.

The Left Border of the Heart.—From above, downward, four contours may be visualized·

1. The aortic knob, formed by the arch of the aorta. Just below this a small portion of the descending aorta may be visible.

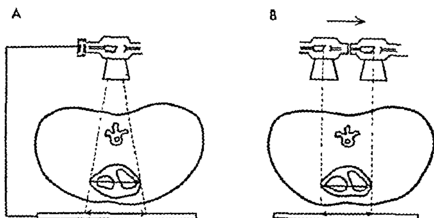


Fig 5 —*A*, Fluoroscopy The diagram shows how the divergent *x*-rays form an image on the fluoroscope screen *Notice that the transverse diameter of the heart as viewed* on the fluoroscope screen is larger than the actual diameter of the heart The fluoroscope screen and the *x*-ray tube move as one unit

B, Orthodiascopy The diagram shows how the central rays of the *x*-ray tube are used to outline exactly the borders of the heart The *x*-ray tube moves, but the fluoroscope screen remains stationary

2 The convex margin of the pulmonary artery and its left main branch lie below the aorta.

3. Below this is the left auricular appendage, which normally cannot be distinguished from the pulmonary artery above, or the left border of the left ventricle below.

4. The convex border of the left ventricle slopes down to the diaphragm. At the level of the diaphragm, a small triangular fat pad may be present.

The Inferior (Diaphragmatic) Border of the Heart.—This is usually not distinct. It is formed by the apex and lower border of the left ventricle, the lower border of the right ventricle and a varying portion of the right auricle.

The Trachea.—The trachea and its bifurcation are usually visible within the upper cardiac shadow *Normally, the angle of the tracheal* bifurcation is less than 90°.

The Hilar Shadows.—The hilar shadows, composed of branches of the pulmonary arteries and veins, lie at each border of the cardiac shadow, just below the bifurcation of the trachea. The left hilar shadow is slightly higher than the right

The Esophagus.—The esophagus can be visualized by giving the patient barium paste to swallow. The esophagus has a sharp convexity to the right

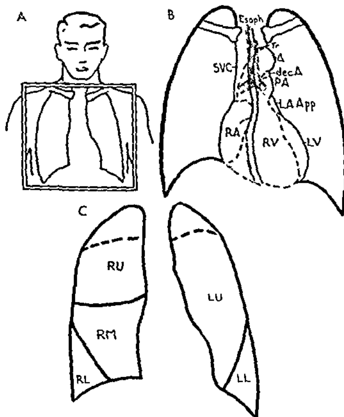


FIG 6.—The normal heart in the posterior-anterior, P-A, position
A, Position of the patient behind the fluoroscope screen
B, Outline of the cardiac chambers A, aorta, dec A, descending aorta, Esoph, esophagus, LA App, left auricular appendage, LV, left ventricle; PA, pulmonary artery; RA, right auricle, RV, right ventricle; SVC, superior vena cava; Tr., trachea.
C, Outline of the lobes of the lungs LL and RL, left and right lower lobes, LU and RU, left and right upper lobes, RM, right middle lobe

at the level of the aorta, where it is compressed by the aortic arch. Below, another gentle convexity to the right may appear, produced by the normal left auricle.

B. The Right Anterior Oblique (R.A.O.) Position (Fig. 7).—The patient turns (to his left) so that his right shoulder touches the screen The patient should turn approximately 60° or until a clear space is visible between the

heart and the vertebral column If the patient has a small build, his arms can be allowed to remain at the side. Or they can be placed on his head, or on his hips, the elbows being rotated backwards. Anteriorly, a clear space should appear between the heart and the sternum (retrosternal space) and posteriorly, the space between the heart and the spine (retrocardiac

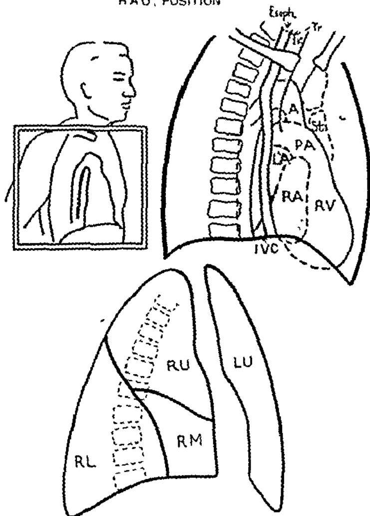


Fig 7 —The normal heart in the right anterior oblique, R A O, position St, sternum Also see caption of figure 6

space) should also be clear. However, the descending aorta lies partially within the retrocardiac space. In addition the retrocardiac space may be partially obscured by pulmonary vessels. This occurs especially in children.

The Anterior Border of the Heart.—*From above down, are the left innominate vein, the ascending aorta, the pulmonary artery, pulmonary conus and wall of the right ventricle If the patient is turned insufficiently,*

that is, less than 45°, the lower anterior border of the cardiac shadow is formed in part by the apex of the left ventricle.

The Posterior Border of the Heart.—The posterior border of the heart, below the aorta and pulmonary artery, is formed by the left auricle, with the right auricle below it. At the diaphragm, a small triangular shadow of the inferior vena cava is sometimes visible.

The superior vena cava, which lies above the shadow of the left auricle, and forms the posterior upper border of the heart, is obscured by the trachea. The shadow of the right innominate vein can sometimes be seen running upward and backwards from the heart and crossing the trachea and the aortic arch.

A small circular density, the pulmonic spot or "fleck pulmonale" can sometimes be seen in the upper portion of the cardiac shadow. This represents the left pulmonary artery, seen on end.

The Esophagus.—The course of the esophagus is usually studied in the right anterior oblique position The patient is given a tablespoonful of a thick paste of barium sulfate in his mouth, told to hold it, positioned correctly, and told to swallow, while the examiner studies the contour of the esophagus This can be repeated as often as is necessary. The esophagus runs vertically, with a sharp posterior indentation at the level of the aorta, and a gentle posterior displacement at the level of the left auricle (Fig. 7).

A good approximation of the diameter of the arch of the aorta can be obtained when the esophagus is outlined with barium, because the aorta indents the esophagus here However, the actual arch of the aorta and the descending aorta are poorly visible in the R A.O position.

Trachea.—The trachea is visible within the upper posterior contour of the heart and the descending limb of the thoracic aorta. The left main bronchus runs anteriorly, and the right main bronchus runs posteriorly.

C. The Left Anterior Oblique (L.A O.) Position (Fig. 8).—The patient turns so that his left shoulder touches the screen He should turn approximately 60°, or until the posterior surface of the heart has cleared the spine. Normally the retrosternal space should be clear, and the posterior border of the left ventricle should clear the spine when the patient is turned 60°.

The Anterior Border of the Heart.—The anterior border of the heart in the L A O position, from above downward, consists of the ascending limb of the aorta, the right auricle and right ventricle. The entire arch of the aorta can be traced posteriorly, as well as part of the descending limb of the thoracic aorta, most of which, however, is obscured by the spine. The innominate artery and vein runs vertically upward, beginning at the junction of the ascending aorta and the aortic arch.

The Posterior Border of the Heart.—This is formed by the left auricle and left ventricle, which lie below the aorta and pulmonary artery. A small clear space, the aortic window, occupied by the trachea and bronchi, is visible between the lower margin of the aortic arch and the left main pulmonary artery, which runs obliquely upward and backward from within the cardiac shadow. The aortic triangle, on the other hand, is another translucent area which lies above the aorta. Its anterior margin is the left subclavian artery (Fig. 20, page 77). Its posterior margin is the spine. Its base is the arch of the aorta. Its apex usually lies above the clavicle.

In the L.A.O. position, a notch is sometimes visible on the diaphragmatic surface of the heart. This has been described as the interventricular groove, though it is questionable whether it actually marks the lower end of the interventricular septum. In addition, on the posterior border of the heart in the L.A.O. position, a shallow auriculoventricular groove has also been described.

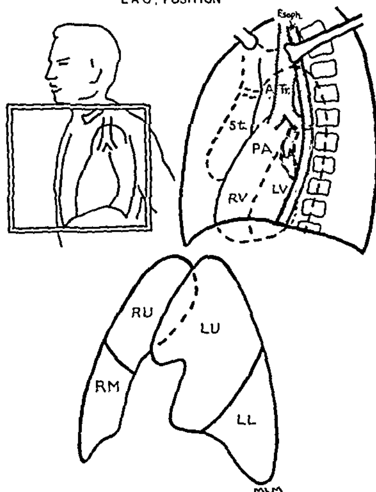


FIG 8 —The normal heart in the left anterior oblique, L A O, position St, *sternum* Also see caption of figure 6

The Trachea.—The trachea is visible within and below the aortic arch The right main bronchus points anteriorly and appears foreshortened The left main bronchus runs obliquely downward and backward and is more vertical than horizontal

The Esophagus.—At the level of the aortic arch the esophagus may show a slight anterior convexity.

Differentiation of the Right Anterior Oblique from Left Anterior Oblique View in X-Ray Films.—When oblique x-ray films of the heart are taken, the following criteria can be used to distinguish the two positions even though the films are not marked:

R A O Position	*L.A O Position*
1 Long axis of heart is oblique	1. Long axis of heart is vertical
2 Heart is pear shaped	2 Heart is globular
3 Aorta is poorly visualized	3 Aorta is well visualized
4 Bifurcation of trachea is indistinct	4 Bifurcation of trachea is distinct, and the right and especially the left bronchus are clearly visualized
5 The anterior border of the heart appears to be adjacent to the thoracic border	5 The anterior border of the heart appears far removed from the thoracic border
6. The magenblasse (gas bubble) of the stomach is visualized "anteriorly" on the film	6 The magenblasse is visualized in the center of the film

ORTHODIASCOPY

Orthodiascopy also utilizes the fluoroscope, but here, the exact contours of the heart are drawn on transparent paper placed in front of the fluoroscope screen This can be done because the point where the central rays emerge from the tube is marked with a small round lead marker, whose image is projected on the fluoroscope screen The screen remains stationary and the examiner moves the tube up and down, and right and left along the borders of the heart, keeping the marker on the borders, and drawing the outline so obtained (Fig 5, *B*, page 58). (In ordinary fluoroscopy, the tube and screen move as one unit.)

Orthodiascopy is valuable because it provides a permanent record of the shape of the heart, but is time-consuming, and requires a high degree of skill Measurement of the transverse diameter of the heart, the area of the heart, *etc* can be made from an orthodiagram (see below).

TELEORADIOGRAPHY

Teleoradiography is the procedure of taking an x-ray film at a standard distance of 2 meters, about 6 feet At such a distance the divergent rays which outline the cardiac shadow enlarge the size of the heart by only from 4 to 12 per cent. The target of the tube is placed at the level of the seventh thoracic vertebra, and exposure is usually made at the end of a normal inspiration, because the size and shape of the heart can vary widely with respiration. (It appears smaller and more vertical on inspiration.)

Films are ordinarily taken in the *P–A* position (the patient is placed with his sternum pressed against the cassette), or in the L.A.O or R.A O position The contours of the heart as seen in the film are the same as those described above for fluoroscopy.

THE EFFECT OF VARIATIONS IN THE POSITION OF THE HEART ON FLUOROSCOPIC AND X-RAY FINDINGS

The heart is not fixed in the thoracic cage and its position can vary widely around several axes (see page 86). In fluoroscopic and *x*-ray examinations it has been customary to describe the heart as horizontal (transverse) or vertical. The horizontal heart appears more squat and slightly larger than the vertical heart Figures 9 and 10 show the differences between a normal horizontal and vertical heart Patients with a horizontal heart often have a prominent apical fat pad which may cause the cardiac shadow to resemble the configuration of a heart with left ventricular enlargement.

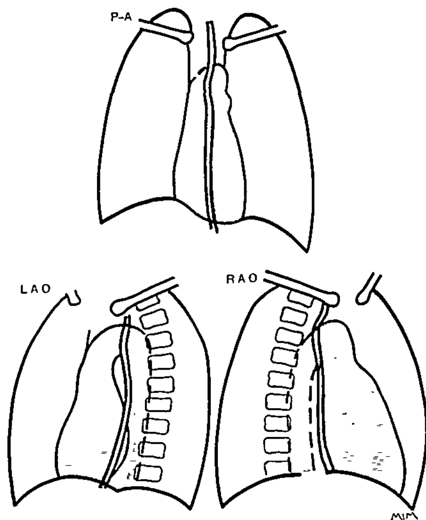


Fig 9 —A normal vertical heart.

Patients with a vertical heart often have a prominent pulmonary artery segment, which in the past, has been misinterpreted by some as a sign of right ventricular enlargement. Further consideration of the effect of the position of the heart on the cardiac silhouette is outside the scope of this book.

CARDIAC MEASUREMENTS

Measurements of the size of the heart can be made from the orthodiagram or the teleoradiogram. These measurements are usually made from tracings or films taken in the P-A position

There are definite relations between height and weight and the transverse diameter of the heart, the surface area of the heart, and the volume

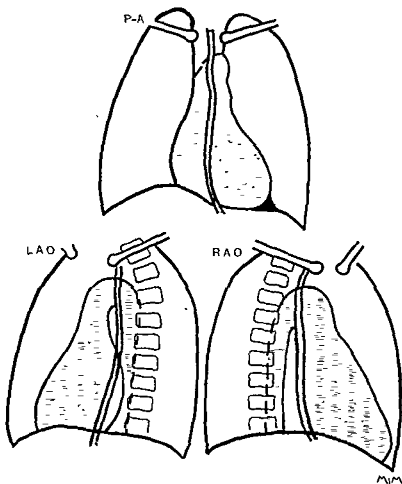


Fig 10 —A normal horizontal heart

of the heart Because of this, tables of normal values have been constructed for use in determining whether cardiac measurements which may appear normal on general inspection are actually within normal limits. Such measurements can also show quantitative changes in the size of the heart. However, even such correlations are far from ideal, and a measurement is not to be considered abnormal unless it exceeds the standard by at least 10 per cent

The Transverse Diameter of the Heart (Fig. 11).—A vertical line is drawn, dividing the chest into equal halves. From this midline, a line, *TR*, is drawn to the outermost portion of the cardiac silhouette on the right, and a line, *TL*, is drawn to the outermost portion of the cardiac silhouette on

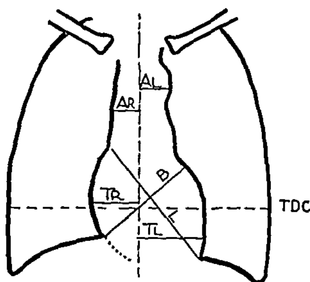


Fig 11 —Diagram showing the diameters used for cardiac measurement AL + AR, width of the aorta, B, broad axis of the heart, L, long axis of the heart, TDC, transverse diameter of the chest The transverse diameter of the heart equals TL + TR

the left. The maximum transverse diameter of the heart is therefore *TR* + *TL*.

With the patient's weight and height as a guide, the nomogram in figure 12, *B*, can then be used to determine if the transverse diameter is normal or not. In adults, the transverse diameter ranges from 10 to 15 cm., depending on size, and in children, from 6 to 10 cm.

The Cardiac Index.—Another measurement that has had considerable popularity is the cardiac index This is obtained by dividing the transverse diameter of the heart, *TR* + *TL*, by the transverse diameter of the chest, *TDC* (Fig. 11). The cardiac index should normally not exceed 0.50 or 0 57 (50 to 57 per cent). In other words, the transverse diameter of the heart is usually less than one-half the transverse diameter of the chest.

The Width of the Aortic Arch.—This can also be measured and correlated with the weight and height of the patient, using the nomogram in figure 12, *B*.

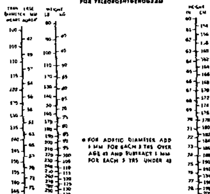
*NOMOGRAMS FOR AREA AND TRANSVERSE DIAMETER OF FRONTAL HEART SILHOUETTE

A PREDICTED AREA FROM WEIGHT AND HEIGHT, AND ACTUAL AREA FROM LONG AND BROAD DIAMETERS

$[A = \pi/4\, L \times B]$ FOR ORTHODIAGRAM AND TELEROENTGENOGRAM

B TRANSVERSE DIAMETER OF HEART AND AORTIC SILHOUETTE PREDICTED FROM WEIGHT AND HEIGHT

FOR TELEROENTGENOGRAM



KEY TO NOMOGRAMS

The values for actual (or predicted) area are read at the point at which a straight line extending from the long and broad diameters (or weight and height) intersects the cardiac area scale. Orthodiagram values are on the left, teleroentgenogram values on the right. In the lower nomogram the predicted transverse diameter of the heart (left side of scale) or aortic arch (right side of scale) is obtained as an extension of a straight line connecting height and weight. A correction for age, as indicated, is necessary for the aortic diameter. Values exceeding 10% above the predicted are abnormal.

FIG. 12.—*A*, Nomogram for measuring the predicted area of the heart from height and weight, and the actual area of the heart from the long and broad diameters. (Kindness of Drs. Ungerleider and Gubner.)

B, Nomogram for determining the predicted transverse diameter of the heart and of the aortic arch from height and weight.

of the heart. Because of this, tables of normal values have been constructed for use in determining whether cardiac measurements which may appear normal on general inspection are actually within normal limits. Such measurements can also show quantitative changes in the size of the heart. However, even such correlations are far from ideal, and a measurement is not to be considered abnormal unless it exceeds the standard by at least 10 per cent.

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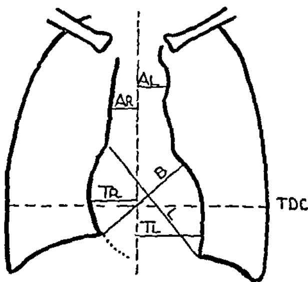


FIG 11 —Diagram showing the diameters used for cardiac measurement AL + AR, width of the aorta, B, broad axis of the heart; L, long axis of the heart; TDC, transverse diameter of the chest The transverse diameter of the heart equals TL + TR

the left. The maximum transverse diameter of the heart is therefore $TR + TL$

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The Width of the Aortic Arch.—This can also be measured and correlated with the weight and height of the patient, using the nomogram in figure 12, *B*.

X-RAY EXAMINATION OF THE HEART IN INFANTS AND CHILDREN (Figs. 13, 14)

In infants, the heart frequently is globular in shape. It may extend almost as far to the right of the sternum as to the left, and neither the pulmonary artery nor the aortic arch can be separated from the general cardiac shadow (Fig. 13). In addition, the size of the heart is relatively larger in relation to the thoracic cage than in an adult, and the heart seems

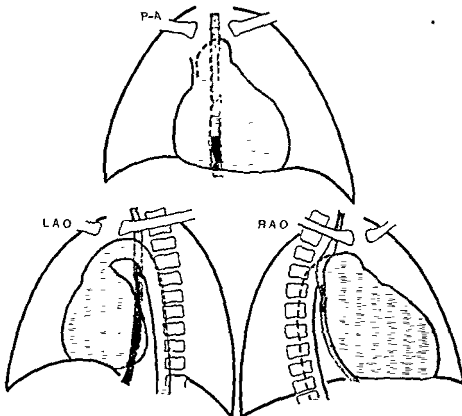


FIG 13 —Normal heart of an infant.

to occupy an inordinately large proportion of the thorax The upper mediastinum may be greatly widened due to the thymus gland. A variation of this picture is a boot-shaped heart with a concave pulmonary artery segment. For fluoroscopic examination, the infant can be given a teaspoonful of barium paste to swallow. If possible, fluoroscopy should be done with the infant lying.

By six months of age, the heart is slightly less globular, but it is not until the age of five or seven years that the configuration resembles that of

an adult (Fig 14). However, even at this age, the pulmonary artery segment remains prominent, and in the R.A.O position, the retrocardiac space may appear clouded, due to prominent secondary pulmonary vessels, giving the erroneous appearance of a large left auricle However, on giving the child barium paste to swallow, the normal configuration of the left auricle will be obvious.

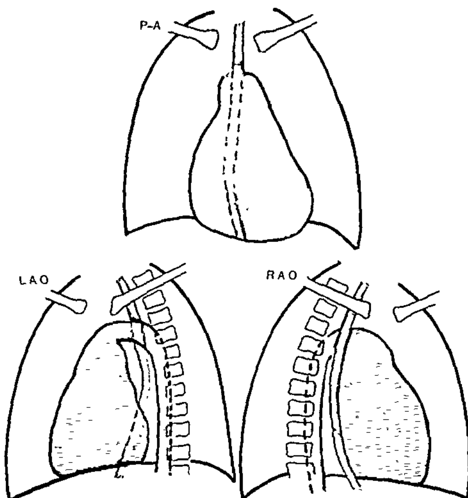


Fig 14.—Normal heart of a child.

ROENTGENKYMOGRAPHY

Roentgenkymography shows the movement of the heart in various phases of systole and diastole on a single *x*-ray film The essential part of the apparatus consists of a large lead sheet in which narrow horizontal slits are cut every 12 mm. apart. Each slit is 0.4 mm. wide. The sheet is called a grid. In the usual method, the film is placed behind the grid, and during

a single exposure of about one and a quarter seconds, the x-ray film slowly moves downward behind the grid a distance of 11 mm., which is 1 mm less than the space between the slits. This leaves a 1 mm. strip of white, unexposed film, which divides the kymogram into frames and prevents overlapping of exposures.

Figure 15 shows a normal roentgenkymogram. During systole, the ventricular portion of the shadow contracts, whereas, over the great vessels, the shadow expands. Roentgenkymography is useful in studying the nature of the cardiac pulsations, and in interpreting the cause of abnormal pulsations. However, much more information about cardiovascular pulsations can be obtained with the electrokymogram.

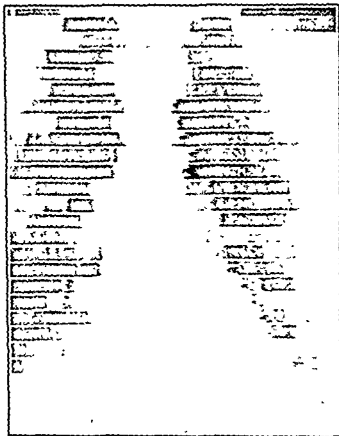


FIG 15 —A normal roentgenkymogram

ELECTROKYMOGRAPHY

The electrokymograph, like the roentgenkymograph, is an instrument which graphically records the movement of the heart and great vessels. The apparatus consists essentially of a photomultiplier tube, a fluoroscope and

an electrocardiograph. The patient is placed behind the fluoroscope screen as for an ordinary fluoroscopic examination. The photo tube is then placed between the patient and the fluoroscope screen with its aperture directed toward the *x*-ray tube *X*-rays which penetrate the patient strike a small fluorescent screen which is mounted over the aperture of the photo tube, and variations in the illumination of this small screen are converted into electrical currents by the tube and then recorded by the electrocardiograph (*Fig. 16*). The purpose of the large fluoroscope screen is to place the photo tube on the desired border of the heart The tracing that results is known as an electrokymogram (EKY) Usually multiple tracings are taken over the ventricles, the auricles and great vessels in the *P-A*, R A O., and L.A.O positions

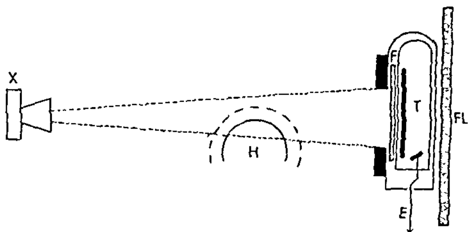


Fig 16—Diagram showing the apparatus used in electrokymography E, Connection to electrocardiograph, F, small fluorescent screen of photo multiplier tube; FL, large fluoroscope screen, H, heart in systole (curved line) and diastole (dotted line); T, photo multiplier tube, X, *x*-ray tube (After Boone *et al*)

In order to time electrokymograms properly, it is necessary to take simultaneously a carotid arteriogram, an electrocardiogram, or a phonocardiogram. For ordinary purposes the carotid arteriogram is preferable. Electrokymograms are usually taken in such a manner that an upward deflection or upstroke indicates an expansile or filling phenomenon of the heart, whereas a downstroke indicates a contractile or emptying phenomenon. A rapid rise or fall of a deflection indicates a rapid action or motion of that particular region of the heart or blood vessel. Electrokymograms are usually taken in the standing position with the patient holding his breath to avoid respiratory movements of the heart.

Standardization of the amplitudes of the deflections of the electrokymogram is difficult because the tracing is due not only to volumetric changes, but to changes in density of the structures, and to changes in the position of the heart, as for example, the motion of the apex toward the base with contraction of the septum, and the wringing motion of the ventricles during systole Changes in shape without changes in volume also affect the electro-

kymogram, as for example, during the isometric phase of systole and diastole.

Figure 17 shows normal electrokymograms of the left ventricle, the right auricle, and the aorta, correlated with the cardiac cycle.

The Ventricular Electrokymogram (Fig. 17).—The ventricular electrokymogram can be analyzed in terms of the cardiac cycle (page 39) in the following way:

Systole.—During the phase of isometric contraction (Fig. 17, 1–2), a slight downstroke occurs because the shape of the heart becomes more globular,

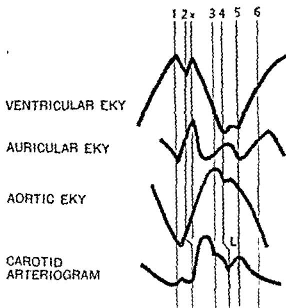


Fig. 17.—Normal ventricular, auricular, and aortic electrokymograms (EKY) timed with the carotid arteriogram. L, Represents the correction factor for lag of the carotid recording system and the pulse wave transmission time. The vertical lines and numerals indicate phases of the cardiac cycle (see text).

although *the volume of the heart remains unchanged.* During the ejection phase (2–3), immediately after the opening of the semilunar valves, the ventricles move outward due to a positional shift of the heart. However, at point *x*, figure 16, a sharp downward deflection occurs as ventricular emptying is accelerated during the phase of maximum ejection. The downward deflection becomes less steep during the protodiastolic phase (3–4), just before the semilunar valves close.

Diastole.—During the isometric phase of relaxation (4–5), *the downstroke may continue, or a biphasic or upward deflection may appear.* However, the tracing rises rapidly during the phase of ventricular filling (5–6). The slope of the tracing then becomes less abrupt during the phase of de-

creased ventricular filling (diastasis), but continues to rise until the onset of the next ventricular systole.

The electrokymogram of the right ventricle is similar to that of the left ventricle.

The Aortic Electrokymogram (Fig. 17).—The electrokymograms from the ascending aorta, the aortic knob and the pulmonary artery are very similar. With the onset of ventricular ejection, a sharp upstroke of the tracing occurs, which reaches its peak near midsystole, and resembles that of the carotid arteriogram (see page 53). In this connection one should remember that the onset of the sharp upstroke in the aortic electrokymogram occurs earlier than in the carotid arteriogram for two reasons: first, the pulse wave has to travel from the aorta to the carotid artery, secondly, there is a lag in the transmission of the pulse wave from the carotid artery to the recording apparatus, depending on the length of the tubing which connects the receiver on the carotid artery to the recording apparatus.

The Auricular (Atrial) Electrokymogram (Fig 17).—Marked variations in the normal auricular (atrial) electrokymogram may occur for the following reasons: the auricular walls may move with auricular systole, or because of transmitted motion from adjacent structures, or from movement of the heart as a whole. A small downward deflection often occurs with auricular systole. The deflection then rises with the isometric phase of ventricular systole, due to a change in the position of the auricles. A second negative auricular deflection occurs with the ejection phase of ventricular systole, but during the middle of ventricular systole, auricular filling becomes sufficient to produce an upstroke of the tracing. The third downward auricular deflection begins with the closure of the semilunar valves, and ends with the opening of the *a–v* valves. At this point, an upstroke occurs even though the *a–v* valves are open and blood is entering the ventricles. This upstroke continues until the next auricular systole

The electrokymogram of the left auricle (atrium) resembles that of the right auricle in a general way, but pure left auricular tracings are difficult to obtain.

ANGIOCARDIOGRAPHY

Angiocardiography (cardioangiography) or contrast visualization of the chambers of the heart, is carried out by the rapid intravenous injection of a radioopaque substance such as 70 per cent diodrast, which makes the cardiac chambers and intrathoracic vessels opaque to *x*-rays. Simultaneously, serial, overpenetrated *x*-ray films are taken every one or two seconds for eight or ten seconds.

The procedure is complicated and requires a special casette changer or photographic device and at least two people, a physician to make the injection, and a technician to take the films. About 35 to 45 cc. of diodrast is used for adults; from 8 to 25 cc. for infants and young children. The injection is very rapid—40 cc. should be injected through a special 12 gauge needle in not more than one and one half seconds. Patients should receive an intraocular or intracutaneous test for sensitivity to the diodrast before the procedure is carried out.

Angiocardiography has proven of value in determining the chambers which form the borders of the heart, and in helping diagnose congenital heart lesions and intrathoracic masses, such as tumors, aneurisms, *etc* It is usually performed with the patient standing in the L.A.O. position, which clearly shows the right and left ventricles and the aorta. The *P-A* position generally gives the clearest visualization of the superior vena cava, the hilar vessels and the left auricle. Angiocardiography can also be carried out with the patient lying.

The following is a brief description of the chambers and vessels which are visualized by angiocardiography ·

THE NORMAL ANGIOCARDIOGRAM

IN THE POSTERIOR-ANTERIOR, P-A POSITION

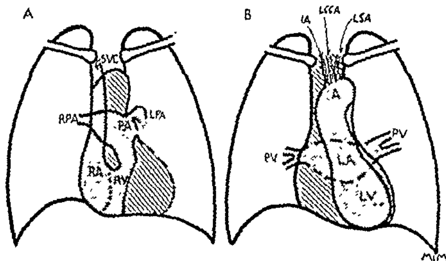


Fig 18 — Normal angiocardiogram in the P-A position *A*, Right heart visualized *B*, Left heart visualized.

A, Aorta, IA, innominate artery, LCCA, left common carotid artery; LPA, and RPA, left and right pulmonary arteries; LSA, left subclavian artery, PV, pulmonary veins, SVC, superior vena cava

P-A Position (Fig 18).—*A*. At about one to three seconds, the right side of the heart, including the superior vena cava, the right auricle and ventricle, and the pulmonary artery appear, U-shaped, within the cardiac silhouette (Fig. 18, *A*). The superior vena cava and the right auricle form the right border of the heart, the right auricle resting on the diaphragm. The right ventricle has a short horizontal and a long vertical segment Occasionally the tricuspid valve region may be identified by a constriction between the right auricle and the horizontal segment of the right ventricle. A constriction may also be present on the vertical segment of the right ventricle in the region of the pulmonary valve, above which is the pulmonary artery The interventricular septum lies more or less vertically, with a convexity to

the right. The conus of the right ventricle, like the main muscle mass of the right ventricle, is centrally located and does not extend to the left border of the cardiac silhouette. However, a small portion of the pulmonary artery and a portion of its left main branch does extend to the left border of the heart, forming the pulmonary artery segment, below the aorta

B At from seven to eleven seconds, when the left heart is opacified, the left auricle is seen as a circular shadow within the cardiac silhouette, along with one or more of the four pulmonary veins emptying into it The main body of the left auricle *usually does not project either to the right or left* border of the heart, but the left auricular appendage does project to the left border, just below the pulmonary artery, where it may or may not be visualized.

The left ventricle appears below and to the left of the left auricle. A constriction between left auricle and left ventricle may appear in films taken *before the aorta becomes opacified* *This is the location of the mitral* valve. Above both the left auricle and ventricle is the ascending aorta and the aortic arch, from which arise the innominate, left common carotid, and left subclavian arteries. A small portion of the descending aorta may be seen on the left border of the cardiac silhouette, above the pulmonary artery.

R.A.O. Position (Fig. 19).—*A* The right heart is visualized as a U-shaped structure and resembles the pattern found in the *P–A* position, except that the limbs of the U are farther apart (Fig. 19, *A*).

Posteriorly, the superior vena cava can be traced into the right auricle, which rests on the diaphragm The right ventricle forms the horizontal and ascending portions of the U. The tricuspid region may be identified by a constriction between the right auricle and the horizontal segment of the right ventricle. Another constriction may be visible on the ascending segment of the right ventricle, where the pulmonary valve is located

Anteriorly, the right ventricle forms the lower portion of the cardiac silhouette Above this is the conus of the right ventricle and the pulmonary artery. *The right branch of the pulmonary artery can be seen passing* horizontally backwards towards the spine. The left pulmonary artery appears foreshortened, and its cross-section may be recognized as a small dense circular shadow, within the shadow of the heart, posterior to and just below the ascending aorta.

B. When the left heart is visualized (Fig 19, *B*), the left auricle is seen to lie above and posterior to the left ventricle. A constriction between the left auricle and left ventricle indicates the mitral valve area. Above both the left auricle and ventricle are the ascending and descending limbs of the aorta

L.A.O. Position (Fig. 20).—*A*. When the right side of the heart is visualized, the two vertical limbs of its U-shaped shadow are superimposed on each other and the right auricle lies behind the right ventricle and cannot be separated from it (Fig. 20, *A*). The interventricular septum shows an anterior convexity. A constriction, marking the location of the pulmonary valve, may be seen within the upper portion of the right ventricular shadow. From the right ventricle, the left pulmonary artery runs horizontally backwards towards the spine. The right pulmonary artery appears foreshortened in this view.

THE NORMAL ANGIOCARDIOGRAM
IN THE RIGHT ANTERIOR OBLIQUE, R.A.O., POSITION

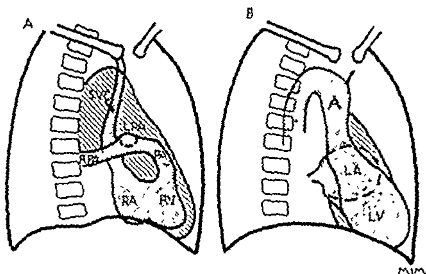


Fig 19 —Normal angiocardiogram in the R A.O position See caption of figure 18

THE NORMAL ANGIOCARDIOGRAM
IN THE LEFT ANTERIOR OBLIQUE, L.A.O., POSITION

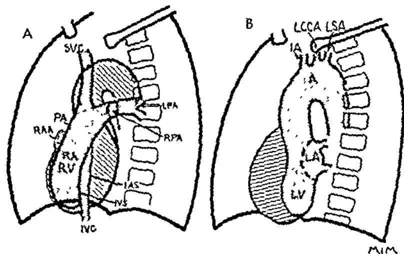


Fig 20 —Normal angiocardiogram in the L A O position IAS, interauricular septum, IVS, interventricular septum; IVC, inferior vena cava, RAA, right auricular appendage Also see caption of figure 18

B. When the left heart is visualized, the left auricle is seen above and posterior to the left ventricle. One or more of the four pulmonary veins may be visualized *emptying into the left auricle. The aorta arises from the left* ventricle, in front of the left auricular shadow. The ascending limb, arch, and descending limb of the aorta are visualized as well as the innominate, left common carotid and left subclavian arteries.

Lateral Position. – In this position, the cardiac chambers and vessels are visualized as in the left anterior oblique position However, the pulmonary conus reaches the anterior border of the heart.

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Chapter 4

ELECTROCARDIOGRAPHIC EXAMINATION

INTRODUCTION

When the heart contracts, electrical currents are produced and distributed through the body to the skin These currents can be recorded by a suitable galvanometer, such as an electrocardiograph. Electrodes can be placed on any two points of the body and connected to the two poles of the electrocardiograph galvanometer In the past, it was customary to place electrodes on the extremities in the following way to obtain the standard leads: left arm and right arm (lead *I*), left leg and right arm (lead *II*); left leg and left arm (lead *III*) More recently one electrode was placed on one or more points over the precordium and the other electrode on the left leg or right arm (precordial *CF* or *CR* leads). Since such tracings are obtained from two active electrodes, such leads can be called bipolar leads (Fig. 21, *A*).

Unipolar leads constitute the new method of electrocardiography. Unipolar leads can be obtained because the sum of the electrical potentials which are present at the three extremities equals zero at every instant in the cardiac cycle Thus, if the three extremities are connected together by means of electric wire (into which some cardiographers incorporate fixed resistors of 5000, 10000, 25000 or more ohms to equalize inequalities of skin resistance), the central terminal connecting the three wires together will have a zero (actually a constant) potential, so that when one pole of the electrocardiograph galvanometer is connected to this central terminal and the other pole to any region of the body, the tracing that results can be called a unipolar, V, lead (Fig. 21, *B*)

Unipolar precordial leads (*Wilson leads*) are usually taken from the following six regions:

Lead V_1—the precordial or exploring electrode is placed on the fourth intercostal space just to the right of the sternum.

Lead V_2—the precordial electrode is placed on the fourth intercostal space just to the left of the sternum.

Lead V_3—the precordial electrode is placed midway between the positions of leads V_2 and V_4.

Lead V_4—the precordial electrode is placed on the fifth left intercostal space at the midclavicular line

Lead V_5—the precordial electrode is placed on the left anterior axillary line at the level of lead V_4

Lead V_6—*the precordial electrode is placed on the left midaxillary line at* the level of lead V_4.

Unipolar leads taken from the extremities with the above technic are often so small in amplitude that interpretation is difficult. However, the

amplitudes of the deflections in the unipolar extremity leads can be increased 50 per cent without changing the standardization, by breaking the connection of the indifferent electrode to the extremity being recorded (Fig 21, C). Such unipolar leads are called augmented unipolar extremity leads (*Goldberger leads*): *aVL* (left arm), *aVR* (right arm), and *aVF* (left leg).

Current practice is to take the six unipolar precordial leads, the three augmented unipolar extremity leads, and the three standard leads, although

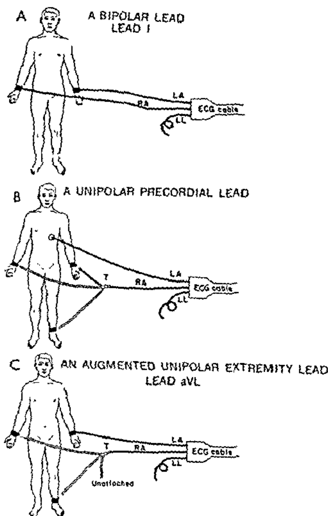


FIG 21 —*A*, Connections for a bipolar lead The connections of lead I are shown
B, Connections for a unipolar precordial, V, lead T, is the central terminal of an indifferent electrode of zero potential
C, Connections for an augmented unipolar extremity lead The connections of the augmented left arm lead, *aVL*, are shown. (In both *B* and *C* the indifferent electrode may or may not contain resistors)

the standard leads do not give any information that is not obtained with augmented unipolar extremity leads, and actually give much less information. However, throughout the book, I shall describe both normal and abnormal electrocardiographic patterns in terms of these twelve leads.

The criteria described for the unipolar precordial leads are generally applicable to the ordinary precordial CF or CR leads. However, minor and sometimes marked variations may occur. For example, a downward P in unipolar lead V_4 signifies a nodal P wave, whereas in precordial lead CF_4, P may be downward even though sinus rhythm is present.

THE NORMAL ELECTROCARDIOGRAM

A normal electrocardiogram is usually described as consisting of a P wave, a QRS complex, an RS-T segment and a T wave (Fig 22, D). Occasionally there is a small round deflection, the U wave, between the T and the next P. Actually it is more accurate to consider the electrocardiogram as representing electrical activity in the auricles and in the ventricles. The P wave represents the spread of the stimulus through the auricles. The

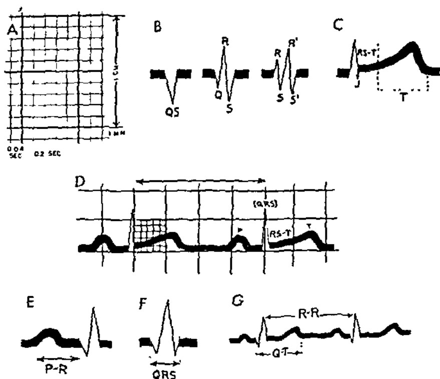


Fig 22 —*A*, Time and amplitude markings of the electrocardiogram
B, Description of the *QRS* complex
C, A normal *RS-T* segment and *T* wave See text
D, Measurement of the heart rate See text
E, Measurement of the *P-R* interval
F, Measurement of the width of the *QRS* complex
G, Measurement of the *Q-T* and *R-R* intervals

return of the stimulated auricles to the resting state produces a shallow, wide deflection, the *auricular T, or Ta wave*, which is usually hidden within the *QRS* complex and the first portion of the *RS–T*. The stimulation of the ventricles produces the *QRS* complex and the return of the stimulated ventricles to the resting state produces the *RS–T* and *T*. The junction between the *QRS* and the first portion of the *RS–T* is called *J* (Fig. 22, *C*)

The normal *P* is usually a small round deflection, but it may be peaked or slightly notched, or occasionally biphasic or downward, as in lead III or aVL

The shape of the *QRS* complex varies greatly depending on the position of the heart, the direction in which the stimulus spreads through the ventricles and on other factors For this reason, the following uniform nomenclature is used to describe the various deflections of the *QRS*, which applies to all leads (Fig 22, *B*)

Q—an initial downward deflection.

R—the first upward deflection. It may be the initial deflection of the *QRS* or may follow a *Q* wave

QS—a *Q* wave not followed by an *R* wave. It forms the entire *QRS* complex.

S—the first downward deflection after an *R* wave

R' and *R"*—additional upward deflections which occur after the first *R*.

S' and *S"*—additional downward deflections which occur after the first *S*.

Small and capital letters can be used to describe the relative sizes of the deflections, as *rS*, *qR*, *QR*, *etc*

The normal *QRS* rises or falls sharply. Small notches (notching) often occur on its ascending or descending limbs Notching is normal Similarly, sudden slowing of the rate of ascent or descent of the *QRS* (slurring) itself is not abnormal but it may be associated with other abnormalities, such as bundle branch block, *etc.*

RS–T.—The normal *RS–T* may or may not lie on the base line Normally, when *T* is upward, the *RS–T* lies above the base line but shows a downward convexity (Fig 22, *C*) When *T* is downward, the *RS–T* often lies below the base line and shows an upward convexity

T.—The shape and amplitude of *T* vary in each lead When *T* is upward, it rises slowly with a downward convexity and abruptly returns to the base line. When *T* is downward, it descends slowly with an upward convexity and abruptly rises to the base line. The peak of *T* is therefore nearer the end of the *T* than its beginning, and *T* is normally asymmetrical (Fig 22, *C*)

MEASUREMENTS OF THE WAVES AND INTERVALS OF THE ELECTROCARDIOGRAM AND THEIR NORMAL VALUES

Normal values for the *P* wave, *QRS* complex, *RS–T* segment, and *T* wave are presented in Table 1, and their measurement illustrated in figure 22. In general, measurements should be made from the lead with the largest or widest complexes, with the exception of the *P–R* interval, where the shortest measurement should be noted The amplitude of an upward deflection is measured from the upper level of the base line to the peak of

the deflection, the amplitude of a downward deflection is measured from the lower level of the base line to the lowest point or nadir of the deflection. When the amplitude of *QRS* (or of a biphasic *P*) is measured, the values of its largest upward and downward deflections should be added. Elevation or depression of *RS-T* is best measured from a point about 0.04 second after *J*, because *J* may be much higher or lower than the rest of the *RS-T*. The base line is best observed just before *P* begins. However, when the heart rate is rapid, *P* may be superimposed on the end of *T* or *U*. In such a case, the interval between *P* and *R* is used as the base line.

Measurements can also be made of the heart rate, the *P-R* and *QRS* intervals, the *Q-T* interval, and the time of onset of intrinsicoid deflections.

The Heart Rate (Fig. 22, *D*).—The heart rate can be measured by counting the number of 0.2 second time intervals between any two successive *R* waves, or *P* waves, and dividing the constant, 300 by this value. The result is the heart rate per minute. A more exact way is to count the number of 0.04 second time intervals between two successive waves and divide the constant, 1500, by this value. Normal values for the heart rate are given on page 319.

The P-R Interval (Fig. 22, *E*).—This represents not only the time it takes the stimulus to spread from the sinus node to the *a-v* node (see page 265), but also the time it takes the *a-v* node to respond to the stimulus. Normal values for the *P-R* interval are given on page 324.

The QRS Interval (Fig. 22, *F*).—This represents the time it takes the stimulus to spread through the ventricles. Normal values for the width of the *QRS* interval are given in table 1.

The Q-T Interval (Fig. 22, *G*).—The *Q-T* interval is sometimes called electrical systole, because it corresponds roughly to the period of mechanical systole in the ventricles. It varies with age, sex and the heart rate, becoming shorter as the rate increases. For correlation of the measured *Q-T* interval with the ideal *Q-T* which should normally occur with any heart rate, the nomogram in figure 23 can be used. Values are given in terms of the *Q-T* ratio which is based on Bazett's formula, $Q\text{-}T = 4\sqrt{R\text{-}R}$. When the measured and ideal *Q-T* intervals are equal, the *Q-T* ratio is 1. When the measured *Q-T* interval is longer than the ideal, the *Q-T* ratio is more than 1, and when the measured *Q-T* is shorter than the ideal, the *Q-T* ratio is less than 1. Theoretically, a *Q-T* ratio of more than 1 should be abnormal. Actually the range of normal values exceeds this. The average normal *Q-T* ratio for men and children is 1.01, and for women, 1.02. The maximum normal *Q-T* ratio for men and children is 1.08, and for women, 1.09.

Intrinsicoid Deflections.—The intrinsic or intrinsicoid deflection is determined from precordial leads. It measures in a general way the time it takes the stimulus to reach a point directly beneath the precordial electrode. It is usually measured from the onset of the *QRS* complex to the peak of the *R* wave. For accuracy a measuring instrument should be used. The maximum time of onset of the intrinsicoid deflection in lead V_1 is 0.03 second; in Lead V_5 or V_6, 0.05 second.

Discussion of the ventricular gradient and other theoretical aspects of electrocardiography is outside the scope of this book. I have also omitted a consideration of axis deviation because of the fallacious conclusions that

Table 1.—Some Normal Electrocardiographic Values.

	Standard Leads	*Augmented Unipolar Extremity Leads*	*Unipolar Precordial Leads*
		P	
Direction	I: may be − in infants II: + III. + or −	aVL + or − aVR: − aVF· +	$V_{1,2}$ ± or − $V_{3,4}$: +
Maximum Amplitude	I: +2 mm II: +2.5 mm III. −1 mm · +2 mm	aVL −2 mm : +2.5 mm aVR· −2.5 mm aVF· +2.5 mm	$V_{1,2}$· +2 mm
Duration	0.6 to 0.11 second	0.6 to 0.11 second	
		QRS	
Direction	See figure 24	See figure 24	See figure 25
Amplitude	$R_1 + S_3 < 25$ mm $S_2 + S_3 < 40$ mm *QRS* at least 5 mm in one lead	aVL: R < 13 mm.* aVF· R < 20 mm * *QRS* at least 4 mm in one lead	
Duration	0.6 to 0.11 second	0.6 to 0.11 second	
		RS-T	
Deviation from Base Line	I: −0.5 mm to +1.5 mm II: Same as I III· −1 mm to +1.5 mm	aVL −0.5 mm to +1 mm aVR −0.5 mm to + 0.5 mm aVF Same as aVL	−0.5 mm. to +2.5 mm
		T	
Direction	I· + II + III: + or −	aVL· + or − aVR· − aVF: + or −	In leads with *rS*, *T* may be −, especially in V_1, but also in $V_{2,3,4}$, especially in children. In leads with *qR*, *T* is +
Amplitude	I· +1 mm to +5.5 mm II +1 mm to +7 mm III· −3 mm to +5 mm	aVL· with a *qR*, −1 mm to +4 mm aVL· with an *rS*, *QS* or *QR*, to −2.5 mm aVR. −1 mm to −6 mm aVF. −1 mm to +5 mm	In leads with *rS*, to −4 mm. In other leads, to +12 mm.

+, Upward deflection; −, downward deflection; ±, biphasic deflection; <, less than, >, more than; *, if *qR* is present.

have resulted from it, especially in regard to left and right ventricular strain and hypertrophy and right and left bundle branch block

THE STANDARD LEADS AND THE AUGMENTED UNIPOLAR EXTREMITY LEADS

These leads vary greatly with the position of the heart The effect of variations of the position of the heart on the electrocardiogram can be summarized very briefly as follows:

1. All hearts can be divided into two groups, vertical or horizontal (When the heart shifts from a vertical to a horizontal position or vice versa, it rotates around the antero-posterior axis of the heart)

2 The heart can also rotate around its long axis. Clockwise rotation occurs when the right ventricle becomes more anterior, and the left ventricle more posterior *The reverse rotation is called counterclockwise.*

3 The apex of the heart can also rotate backward or forward around the transverse axis of the heart

Rotation around any or all of these three axes can cause marked changes in both the normal and abnormal electrocardiogram The position of the *heart can usually be determined from the augmented unipolar extremity* leads. Three of the more important rules used in this connection are as follows.

1 A heart is considered to be vertical when lead *aVL* shows a *QS* or an *rS* pattern. (An exception to this rule may occur after anterior infarction *where lead aVL may show a QS although the heart is horizontal)*

2. A heart is considered to be horizontal when lead *aVL* shows a *qR* or a *QR* pattern.

3 Marked clockwise rotation of the heart is considered to be present when lead *aVR* shows a *Qr*, or a *QR*, or a *qR* pattern

Figure 24 shows some of the more common patterns in both the standard leads and augmented unipolar extremity leads that occur with variations in the position of the heart Normal values of the deflections are given in Table 1.

THE UNIPOLAR PRECORDIAL LEADS

The precordial leads are affected particularly by clockwise or counterclockwise rotation of the heart. Ordinarily, *rS* and *RS* patterns appear near the sternum and *qR* patterns appear on the left side of the chest. The transition between the two patterns usually occurs between leads V_4 and V_5, or leads V_3 and V_4. However, when marked clockwise rotation is present, an *rS* or *RS* pattern may persist even in lead V_5, or V_6 (Fig 25). When counterclockwise rotation is marked, a *qR* pattern may develop in lead V_3 or even in lead V_2 This is very unusual in a normal heart.

The following *T* wave patterns can occur normally in the precordial leads. *T* may be normally upward in all precordial leads. It is often downward in lead V_1, and in children, a downward *T*, in association with an *rS* or *RS* pattern may extend to lead V_4 (the juvenile pattern). This pattern also is found in a small percentage of normal adults In precordial leads with a *qR* pattern, *T* is normally upward. Normal values of the *T* wave are given in Table 1.

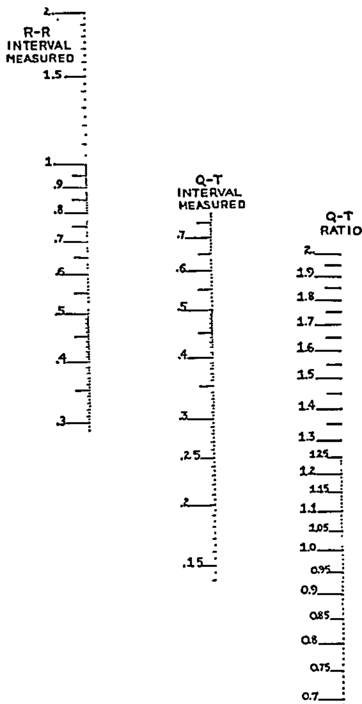


Fig 23.—Nomogram for measuring abnormalities of the *Q-T* interval in terms of the *Q-T* ratio See text

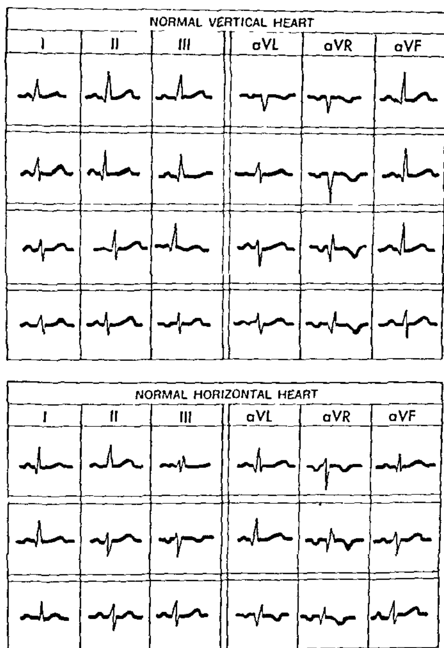


Fig 24 —Normal variations in the standard and augmented unipolar extremity leads

The Electrocardiogram of Children and Infants.—The electrocardiogram of a child is similar to that of an adult. The juvenile *T* wave pattern in the precordial leads has already been mentioned. In the standard and augmented unipolar extremity leads, large *T* waves are common.

In infants, tall *R* waves may appear in precordial leads $V_{1\ 2}$, similar to the pattern which occurs after right ventricular hypertrophy. However, in normal infants, the peak of the *R* occurs quickly, less than 0.04 second after it begins to rise from the base line, whereas if the tall *R* were caused by right ventricular hypertrophy, the peak of the *R* usually occurs 0.04 second or later after its onset. In addition, the normal *P* wave in lead V_1 is small, whereas in congenital lesions in infants, causing right ventricular hypertrophy, a large *P* often appears in lead V_1.

A *QS* and downward *T* may appear in lead I, and in lead *aVL*, the major *QRS* deflection is downward because the normal infant has a vertical heart.

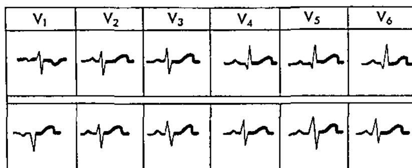


Fig. 25 —Two normal precordial leads

VECTORCARDIOGRAPHY

The **vectorcardiogram,** sometimes abbreviated as *VG*, *VC*, or *VCG*, is merely a curve or loop showing how the electrical axis of the heart varies from instant to instant in a single heart beat. It can be derived from two electrocardiograms or can be obtained directly, using the following:

1. A cathode ray oscillograph (oscilloscope) (which resembles a television apparatus) is used to record the loop, which appears as an image on the face of the oscillograph tube

2. Two pre-amplifiers are necessary to amplify the electrical currents from the heart before they are led into the oscillograph These pre-amplifiers are actually the power units of two electrocardiographs.

3 A camera is needed to photograph the image of the vectorcardiograph loop

In taking a vectorcardiogram, it is necessary to take simultaneously two leads which lie at right angles to each other. For example, in order to obtain a vectorcardiogram from the frontal plane of the body, lead I can

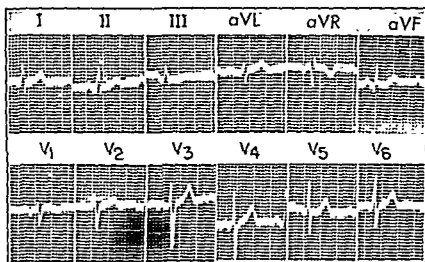


FIG 26.—Normal vectorcardiogram. (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger.)

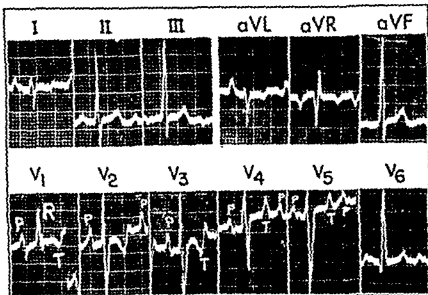


Fig 27 —Vectorcardiogram in right ventricular hypertrophy. (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger)

be taken (this lies on a horizontal plane) and lead aVF can simultaneously be taken (this lies on a vertical plane, at right angles to the horizontal). Both these leads are fed into the oscillograph, and the resultant curve is known as a *frontal plane vectorcardiogram*.

A *horizontal plane vectorcardiogram* can be taken by using lead I and precordial lead V_1 (or lead V_8, at the angle of the left scapula).

A *sagittal plane vectorcardiogram* can be taken by using lead V_1 (or lead V_8) and lead aVF

The vectorcardiogram has a direct relationship to the electrocardiogram, in the following ways.

A *frontal plane vectorcardiogram* is merely a composite cardiogram derived from the standard leads and the augmented unipolar extremity leads. Therefore, abnormalities which occur in the standard and unipolar extremity leads will appear in the frontal plane vectorcardiogram

A *horizontal plane vectorcardiogram* is merely a composite cardiogram derived from the precordial leads Therefore, abnormalities which occur in the precordial leads will also appear in the horizontal plane vectorcardiogram

A *sagittal plane vectorcardiogram* is merely a composite cardiogram derived from esophageal leads Therefore, abnormalities which occur in the esophageal leads will also appear in the sagittal plane vectorcardiogram

Although vectorcardiograms can be taken with a cathode ray oscillograph, the apparatus is cumbersome and expensive. However, vectorcardiograms can be derived in a very easy way from the ordinary electrocardiograms. For example, the *frontal plane vectorcardiogram* can be derived from leads I and aVF, the *horizontal plane vectorcardiogram* from leads I and V_1, the *sagittal plane vectorcardiogram* from leads V_1 and aVF The details of doing this are described in my book, *Unipolar Lead Electrocardiography and Vectorcardiography*.

At the present time, vectorcardiography is mostly of theoretical rather than clinical interest. However, the vectorcardiogram is very helpful in diagnosing right ventricular hypertrophy when precordial leads $V_{1,2}$ do not show the characteristic tall R waves. In such cases, the *horizontal plane vectorcardiogram* will show a clockwise rotation of the vector loop, rather than a normal counterclockwise rotation This change in rotation can be determined from the electrocardiogram, because I have found that when right ventricular hypertrophy is present and the horizontal plane vectorcardiogram has clockwise rotation, the peak of the R wave in lead V_1 will occur later than the peak of the R wave in lead I (In the normal heart, the peak of R in lead V_1 occurs earlier than the peak of R in lead I.)

Figure 26 shows a normal vectorcardiogram occurring in a vertical heart. Note that the *horizontal plane vectorcardiogram* has counterclockwise rotation.

Figure 27 shows a classical example of right ventricular hypertrophy with a clockwise rotation of the *horizontal plane vectorcardiogram*.

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Chapter 5

BALLISTOCARDIOGRAPHIC EXAMINATION

INTRODUCTION

THE term, **ballistocardiogram**, was coined by Starr in 1939. It is derived from the Greek *ballein*, to throw, *kardia*, the heart; *gramma*, a drawing. It is, therefore, a record of the movements of the body produced by the force *of the heart beat*.

Ballistocardiograms are usually recorded by means of an electrocardiograph. However, the ballistocardiogram and the electrocardiogram measure completely different phenomena. The *electrocardiogram* records the changes in electrical potential which develop in the heart muscle during each heart beat. The *ballistocardiogram* represents mechanical events which occur in the body as a result of the heart beat and is actually a measure of the efficiency of the heart as a mechanical pump.

The movements of the body produced by the heart beat can be observed very easily if one stands still on a bathroom scale and watches the movements of the pointer which occur with each pulse. As a matter of fact, this observation was first made by Gordon in 1877, who recorded these movements.

The basic physical principle underlying use of the ballistocardiogram is Newton's third law of motion which states that "for every action, there is an equal and opposite reaction." We are all familiar with the recoil which occurs when a gun is fired. Similarly, in the human, there is a gun (the heart), which fires a projectile (the blood) through a ∩-shaped barrel (the aorta and its tributaries), the whole system being mounted as if on a soft rubber pad.

Figure 28 shows *a normal* ballistocardiogram. *It consists of a series of* deflections or waves which are arbitrarily lettered: *G, H, I, J, K, L, M, N, O.*

H, is an upward deflection and probably represents the recoil of the body from the downward movement of the apex during systole. Auricular systole also contributes to the **H** wave.

I, is a downward deflection and represents the cardiac recoil accompanying *the ejection of blood.*

J, is an upward deflection and represents the deceleration of the blood in its course through the aorta and pulmonary artery. The resistance encountered in the passage of blood through these vessels tends to push the blood back to the heart. **J**, is the recoil of the heart which occurs.

K, is a downward deflection. It is produced in a manner similar to **J**, because as the blood passes to the lower part of the body, it meets resistance which tends to push it back to the heart. **K** is the recoil of the heart that results.

L, M, N, O, are waves of obscure etiology, produced during diastole. Occasionally, a small, downward **G** wave precedes the **H**. The **G** may be due to the recoil from auricular contraction In other cases, an upward **F** wave occurs before the **G** This is also related to auricular contraction

TYPES OF BALLISTOCARDIOGRAPHS

Starr has said that any bright boy with a knowledge of how to work in a machine shop and put together a radio could build himself a ballistocardiograph However, ballistocardiographs range from the simple bathroom scale to a complicated apparatus which uses a seismograph

At the present time there are three main types of apparatus in use:

1 **The High Frequency, Undamped Ballistocardiograph of Starr and Rawson.**—When a semi-rigid object like the human body or a table is

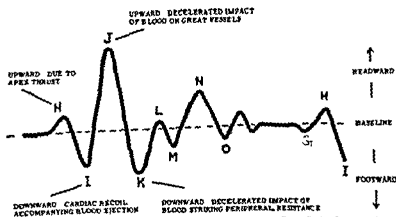


Fig 28 —A normal ballistocardiogram (Kindness of Dr H R Brown, Jr)

struck a blow, or receives an impact from the expulsion of blood, it will be displaced However, instead of returning immediately to its original position, it will tend to vibrate at a particular frequency for a short period of time. The natural frequency of vibration of the body (cadaver) is about 6 cycles per second If the body is placed on a table which has a similar natural frequency, the simultaneous vibrations of the body and the recording table may produce resonance and may cause artificial augmentation of the tracing if the vibrations produced by the heart beat are in phase with this natural frequency However, at other moments, the natural vibrations of the body and recording table may extinguish other vibrations produced by the heart For this reason, it is necessary to have the natural frequency of the recording table as far as possible removed from the natural frequency of the body lying on it.

The Starr apparatus has a high natural frequency of about 15 cycles per second Basically, it consists of a wooden table mounted on four strips of spring steel on a rugged wooden frame. The apparatus is arranged

so that the table can be displaced only in a headward or footward direction A pick-up converts the mechanical movements of the table into an electrical current which is recorded.

2. **The Low Frequency, Critically Damped, Ballistocardiograph of Nickerson.**—This consists of a special table which has a natural frequency of 1.5 cycles per second This is slower than that of the human body This ballistocardiograph table is critically damped so that oscillations produced by one heart beat do not interfere with each other or with those of the next beat The table consists of a board, supported by four long, heavy, flat and adjustable steel springs damped with a special bellows type damper. Its movements are recorded electronically

Nickerson and Curtis believe that the low frequency table gives more accurate records because high frequency ballistocardiographs overaccentuate (by resonance and other factors) the high frequency components of the cardiac cycle to the detriment of the lower frequency events more closely related to the cardiac stroke. Theoretically, this may be so. However, the low frequency of the normal respiratory movements interferes with the oscillations of the Nickerson table so much that the subject must hold his breath while a record is being taken. The subject can breathe normally on the Starr bed.

There are other differences between the Starr and Nickerson ballistocardiographs. The tracings obtained with one are not identical to those obtained with the other One reason for this is that the high frequency Starr ballistocardiograph table is constructed with very stiff springs, giving it a relatively high natural frequency, so that one actually is measuring the force necessary to hold the patient stationary. In other words, the record obtained is a measure of the force of the heart beat On the other hand, the Nickerson low frequency table is constructed with weak springs and it permits the patient to move relatively freely in space. Consequently, the record obtained is a measure of body displacement caused by the heart beat, rather than the force of the heart beat This difference will be mentioned again below when the **displacement, velocity and acceleration** types of direct body ballistocardiographs are discussed

3 **Direct Body Ballistocardiographs.**—Direct body pick-ups are much more simple than the table type ballistocardiographs just described and can be easily used for clinical purposes. In most cases, the direct body ballistocardiograph records the motions of a bar or cross-piece laid across the shins of a patient who lies supine on a rigid examining table

Direct body ballistocardiographs are of three types:

A. **Displacement Type Ballistocardiographs.**—The amplitude of the waves obtained is dependent on how far the body is moved by the force of the heart beat. This apparatus does not measure accurately the force of the heart beat itself, nor does it measure the velocity with which the blood is being ejected.

Displacement type ballistocardiographs are in common use. The photoelectric cell ballistocardiograph of Dock and Taubman is of this type. In this method, a light source is set up so that the amount of light hitting the photo cell is increased or decreased by movements of the body due to the heart beat. One method of accomplishing this is to attach a

cross-bar to the shins so that the cross-bar edge partially hides the source of light. The photo cell is directly connected to an electrocardiograph which records the ballistocardiographic waves

The *displacement* type ballistocardiograph gives tracings similar to those obtained with the Nickerson table It is particularly valuable for recording waves of low frequency. Thus, clinically, it has value in the study of *the normal H wave, respiratory movements, and in the diagnosis of* coarctation of the aorta

B. **Velocity Type Ballistocardiographs**—This apparatus of Dock uses a coil which is placed within the lines of force of a permanent magnet One popular method is to have the magnet anchored rigidly and have the coil mounted across the subject's shins. When the body moves, the coil moves with it, cuts the lines of force of the magnet and generates an electric current which can be very easily recorded using an electrocardiograph.

This method measures velocity because current will flow only when the coil is moving and will cease to flow when the coil comes to rest Tracings obtained are similar to but not identical to those obtained with the *displacement* type apparatus.

C. **Acceleration Type Ballistocardiographs.**—Theoretically, the most important component of the ballistocardiogram is the force imparted to the body by the recoil of the heart. *Neither the displacement type ballisto*cardiograph nor the *velocity* type gives a true indication of this. However, a direct body type of ballistocardiograph which measures the acceleration of the body when it moves as a result of the heart beat is now available. Such an apparatus can be calibrated to measure the force of the heart beat because the acceleration varies with the *force* of the heart beat Direct body ballistocardiographs which can record *displacement, velocity* and *acceleration* in a single instrument are also now available commercially

The *acceleration* type ballistocardiogram gives tracings similar to those obtained with the Starr table It is therefore particularly valuable for recording waves of high frequency. Thus, clinically, it has value in study of the normal *I, J, K*, waves and in studying notches on these waves The ultimate value of the *acceleration* type ballistocardiogram has not yet been determined

When *displacement, velocity,* and *acceleration* ballistocardiograms are taken simultaneously, variations in both the amplitude and shape of the waves will be noted, because high frequency waves may not appear in the *displacement* tracing and low frequency waves may not appear in the *acceleration* tracing In addition, the peaks of the waves do not occur simultaneously The peak of the *acceleration* wave occurs before the peak of the *velocity* wave, and the peak of the *velocity* wave occurs before the peak of the *displacement* wave The peak of the *displacement* wave will occur simultaneously with the nadir of the *acceleration* wave, at which time the velocity curve is at the base line (Fig. 29) (Electrical engineers describe this by stating that the *acceleration* curve is 90 degrees ahead of the *velocity* curve and 180 degrees ahead of the *displacement* curve)

Figure 30 shows why there is asynchronism between the *displacement* and *velocity* curves and why the peak of the curve in the *velocity* tracing occurs earlier than in the *displacement* ballistocardiogram.

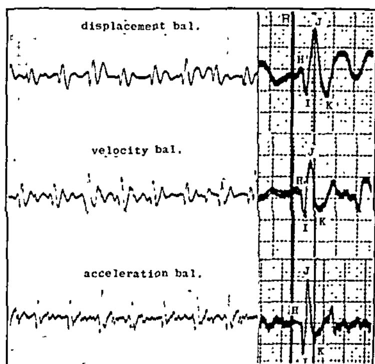


FIG. 29 —Normal displacement, velocity and acceleration ballistocardiograms (after Arbeit and Lindner) *H*, *I*, *J*, *K* are waves of the ballistocardiogram *R*, represents the time of occurrence of the peak of the *R* wave of the electrocardiogram See text for details

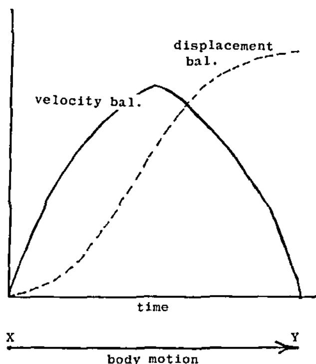


FIG 30 —A comparison of the displacement and velocity ballistocardiograms (after Biber and Lewis). See text for details

The line $X \longrightarrow Y$ represents the movement of the body produced by one heart beat during systole At X, the body is at rest, and after moving to position Y it is again at rest.

When this motion is recorded as a *velocity* ballistocardiogram, the curve resembles the solid line in the figure. It begins at the base line because, at the start, the velocity is zero The velocity gradually increases as more and more blood is forced out of the ventricles, and the curve rises Then the velocity gradually decreases and comes to a halt at the end of systole and the curve correspondingly slowly falls to the base line again.

The *displacement* ballistocardiogram, on the other hand, responds only to the distance the heart moves from point X Thus, at the instant the body reaches point Y, the *displacement* curve (the dotted line) will show its maximum amplitude. At this instant, the *velocity* curve has already reached the base line.

A similar relationship can be shown between the *velocity* and *acceleration* ballistocardiograms

THE NORMAL BALLISTOCARDIOGRAM

In interpreting a ballistocardiogram, one should notice the following: 1, regularity of the ballistic pattern from beat to beat, 2, definiteness of the complexes, 3, the effect of respiration, 4, the amplitude of the individual waves, and 5, constancy of the HK interval

The normal ballistocardiogram shows the following:

1 *Regularity of the Ballistic Pattern from Beat to Beat*—The normal ballistocardiogram shows a regular pattern which does not change from beat to beat, except for slight variations in amplitude which occur with respiration (see below)

2. *Definiteness of the Complexes*—The beginning of each normal complex is definite. However, when the rate is rapid, the H wave may be obscured by oscillations from the previous heart beat In any case, the normal HI stroke is always obvious

3 *Minimal Respiratory Variations.*—The normal ballistocardiogram varies only slightly with respiration During *inspiration* the amplitude of the waves is larger than during *expiration* The reason for this is as follows. First, the heart becomes vertical with inspiration and causes a change in the force of the apex thrust, which is now directed in a more head-to-foot direction. This increases the amplitude of the H wave. Secondly, inspiration causes an increase in the total stroke volume of the heart in the following way: inspiration increases the venous return to the right heart by decreasing the intrathoracic pressure This allows a greater venous return to the right ventricle and the right ventricular stroke volume increases Inspiration also causes the venous return to the left ventricle to diminish, but this is less than the increased venous return to the right ventricle As a consequence, the stroke volume of the entire heart, and the amplitude of the ballistic waves, increase on inspiration During expiration, the reverse changes occur.

The respiratory variations in the ballistocardiogram can be used to differentiate abnormalities of the right or left ventricle During inspira-

tion, the ballistocardiogram can be considered as a right ventricular ballistocardiogram, *during expiration, a left ventricular ballistocardiogram.* This is the reason that abnormalities in the force of left ventricular ejection are masked during inspiration and may be observed only during expiration, when the effect of the right ventricle is decreased.

These respiratory changes are not marked because the lungs act as a reservoir from which the left ventricle can drain to furnish enough blood for an adequate circulation. However, during a prolonged expiration, such as occurs in prolonged sneezing, coughing, or sighing, this pulmonary reservoir can become depleted and syncope may result. In such cases, the prolonged expiration is associated with very small ballistocardiographic waves.

Abnormal respiratory variation can be considered to be present when the IJ amplitude of expiration is approximately one-half or less than in inspiration.

Abnormal conditions which are associated with abnormal respiratory variations in the ballistocardiogram are described on page 216.

Amplitude and Characteristics of the Individual Waves.—The normal ballistocardiogram should show the sequence of *H, I, J, K* clearly defined. In general, the normal individual waves vary as follows:

The H Wave.—The *H* wave can vary markedly in the normal. It can be flat, low, or high. Usually, its peak is less than the depth of *I* and approximately one-fourth the height of *J*.

The I Wave.—The depth of *I* is usually greater than the height of *H* and less than the height of *J*. However, the depth of *I* varies from person to person. *I* normally shows a sharp nadir.

The J Wave.—*J* is the tallest wave. The *IJ* stroke is the highest normal upward deflection and it is an index of the stroke volume of the heart and the force of cardiac ejection. (However, standardization of the ballistocardiogram and the use of complex formulæ are needed to measure stroke volume or cardiac output from the ballistocardiogram.)

The K Wave.—Normally, the *JK* stroke is the mirror image of the *IJ* stroke. *K* is often deeper than *I*, especially on expiration. The *JK* segment is straight, but it normally may be slurred or notched when the heart rate is slow.

Normal variations of *L, M, N,* and *O,* have not yet been described in detail. *N* may be higher than *L*. However, no diastolic wave is normally higher or deeper than the largest systolic wave.

In interpreting the waves of the ballistocardiogram, one must not forget that the use of a *displacement, velocity* or *acceleration* apparatus itself, will cause variations in the shape and amplitude of the waves (page 98, Fig. 29).

Normally, the peaks of the waves of the *displacement* ballistocardiogram occur approximately 0.02 second after the peaks of the *velocity* ballistocardiogram, and the peaks of the *velocity* ballistocardiogram occur approximately 0.02 second after the peaks of the *acceleration* ballistocardiogram.

5. *Constancy of the HK Interval.*—The *HK* interval is measured from the apex of the *H* wave to the nadir of the *K* wave. It represents the duration of the cardiac cycle from the beginning of mechanical auricular systole to the

moment the blood is decelerated by the narrow peripheral arteries It varies from person to person, but it remains constant to 0 01 or 0 02 second in the same person.

Correlation of the Ballistocardiogram with Other Cardiac Events —Figure 31 shows the relations between the *displacement* ballistocardiogram and

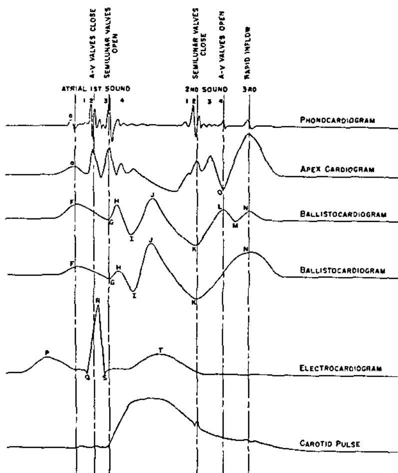


FIG 31.—Time relations of the ballistocardiogram, electrocardiogram, phonocardiogram, apex cardiogram and pulse tracing Two ballistocardiograms have been shown because no one ballistocardiogram shows all the above relationships (after Thompson, Rappaport and Sprague)

the electrocardiogram, the heart sounds and apex pulse tracings These relations will not hold for the *velocity* or *acceleration* ballistocardiograms whose peaks occur before the displacement peaks (see page 97)

Notice that the QRS complex of the electrocardiogram occurs just before the H wave of the ballistocardiogram This relationship can be used to identify the ballistoc

because one lead of the electrocardiogram can be taken simultaneously with the ballistocardiogram, the peak of the *QRS* complex being recorded as a small spike superimposed on the ballistocardiogram

In cases where the *P-R* interval is prolonged, the *QRS* complex may occur after the *H* wave

The Effect of Age on the Ballistocardiogram.—The amplitude of the tracing decreases in old age In addition, the *I* and *J* waves diminish, but the *K* remains deep

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Chapter 6

TESTS OF CIRCULATORY EFFICIENCY

CARDIAC OUTPUT

THE metabolic activities of the body are limited by the available oxygen supply to the tissues. Since oxygen is transported and delivered to the tissues by means of the hemoglobin in the red cells and the oxygen dissolved in the blood plasma, an increased demand for oxygen will necessitate an increased blood flow through the tissues, and an increased outpouring, or output of blood from the ventricles, and the amount of oxygen supplied to the tissues will vary with the oxygen consumption of the tissues, or more specifically, with the metabolic rate. *Thus, when oxygen consumption is high, as in hyperthyroidism or exercise, etc., the cardiac output increases.* When metabolism is low, as in myxedema, or at rest, the reverse occurs.

The relation between metabolic rate and cardiac output is not exactly proportional. For example, in different forms of exercise, the oxygen consumption may be identical but the cardiac output will vary. Similarly, in hyperthyroidism, the cardiac output may be increased out of proportion to the metabolic rate.

Cardiac output may be defined more precisely as the amount of blood discharged from either the right or left ventricle per minute. This assumes that *the outputs of the right and left ventricles are equal. Normally this is so, but discrepancies occur for example in cases of aortic insufficiency,* where the output of the left ventricle is greater than the output of the right ventricle by the amount of blood regurgitating, which may be considerable. Similarly, in cases of congenital heart disease with shunts between the right and left hearts, the output of the left ventricle may be greater than the output of the right (tricuspid atresia), or the right ventricular output may be greater than the left (some cases of simple interventricular septal defects). The amount of blood discharged from the heart per beat is known as the systolic discharge, or the stroke volume. The cardiac output is *therefore simply the product of the stroke volume and the heart rate.*

Cardiac output can be caused to vary in the following ways:

1. By increasing the heart rate. This is effective up to a certain point. However, if the heart beats too rapidly, the duration of diastole and ventricular filling is shortened, so that with each beat, less blood is expelled from the ventricles. It has been found that the maximum rate to which a normal heart can be speeded to increase the cardiac output is from 170 to 180. Beyond this, an increased rate may actually decrease the cardiac output because of the marked decrease in stroke volume that occurs.

2. By increasing stroke volume. This can increase threefold during severe exercise, for example.

One of the mechanisms which produces both the increased heart rate and the increased stroke volume is an increased venous return to the heart. With exercise, for example, the flow of blood through the muscles is greatly increased, and an increased amount of blood is massaged out of the veins toward the right heart by the contracting muscles. This muscular activity produces an increased venous pressure, which in turn, causes the heart rate to increase by way of the Bainbridge reflex. (Bainbridge showed in animals that he could make the heart rate increase by an infusion of saline or blood, which increased the venous return and raised the venous pressure He demonstrated that the heart rate was increased reflexly because it did not appear after section of the vagus and accelerator nerves. Whether the reflex is initiated by the increased venous pressure as Bainbridge believed, or by some other mechanism, is still unknown.)

Exercise further increases the venous return because blood is withdrawn from depots, such as the skin, spleen, *etc*, and the circulating blood volume increases greatly

3 By increasing the oxygen utilization by the tissues. Normally the arterial oxygen content is 19 volumes per cent (19 cc oxygen in 100 cc. arterial blood), and the mixed venous blood coming to the lungs contains about 14 volumes per cent With severe exercise, the oxygen content of mixed venous blood may decrease to 7 or 8 volumes per cent, and even to 3 or 4 volumes per cent in extreme exercise.

The extent to which these three factors operate to satisfy the oxygen requirements of the body varies in person to person, and even in the same person. For example, in athletes, the resting stroke volume may be 120 to 130 cc., double that of an ordinary person, so that, on exercise, the athlete increases his cardiac output without the great increase in heart rate which occurs ordinarily.

An increase in cardiac output usually results in an increase in the work of the heart, which is the product of the cardiac output and the mean arterial pressure.

Measurement of Cardiac Output.—In 1870, Fick showed that the cardiac output could be determined if the oxygen (or the carbon dioxide) content of arterial and mixed venous blood were known, in addition to the total oxygen intake (or carbon dioxide elimination) per minute using the following equation:

$$\underset{\text{(cc per minute)}}{\text{cardiac output}} = \frac{O_2 \text{ intake, cc per minute}}{\text{art. } O_2\text{, vol.\%} - \text{ven. } O_2\text{, vol.\%}} \times 100$$

Thus, if the oxygen content of arterial blood is 19 volumes per cent, the oxygen content of mixed venous *blood is 14 volumes per cent and the oxygen* intake per minute is 300 cc., it follows that every 100 cc. of mixed venous blood reaches the lungs carrying 14 cc. oxygen, and leaves with 19 cc. Therefore every 100 cc. blood takes up 5 cc. oxygen. Since 300 cc. oxygen are taken up in a minute, this is equivalent to a blood flow through the lungs (from the right ventricle) of:

$$5\ 100 = 300.X$$

$$X = \frac{30000}{5} = 6000 \text{ cc. or 6 liters per minute.}$$

In the past, the practical difficulty of using this formula to measure cardiac output has been that no adequate method of obtaining mixed venous blood was available. A sample of mixed venous blood can only be obtained from the right auricle or ventricle, because the venous blood from each extremity contains varying quantities of oxygen (and carbon dioxide), depending on local muscular activity and other local conditions. Thus, until the method of catheterization of the right heart was developed, the Fick formula could not be directly applied to the human Catheterization of the right heart is done by introducing with aseptic precautions, a No 8F or 9F radioopaque catheter, 100 cm., long, with a slightly curved tip, into the antecubital vein and guiding it, under fluoroscopic observation, into the pulmonary artery.

Oxygen intake can be directly measured with the apparatus used for basal metabolism determinations. Arterial blood can be obtained by puncturing a major artery, such as the femoral artery. The arterial and venous blood is collected under oil, and the oxygen content determined by means of the gasometric method of Van Slyke, or photo-electrically.

Cardiac output can also be measured with a calibrated ballistocardiograph table.

Normal Variations in Cardiac Output.—The normal basal cardiac output (with the subject recumbent and at rest, the room temperature 20° C., and twelve hours after eating or drinking) varies from 3 to 5 liters/min. and is related to the surface area of the body, just as the basal metabolism is related to surface area. The cardiac output varies from 2 3 to 4.1 liters per square meter of body surface.

Exercise, excitement, eating, fever—any factor which increases metabolism—increases the cardiac output. Moderate changes in environmental temperature do not greatly affect the cardiac output. Postural changes affect the cardiac output, which falls on standing This is due to the pooling of blood in the lower extremities.

CIRCULATION TIME AND THE SPEED OF BLOOD FLOW

Generally speaking, the cardiac output varies with the speed or velocity of blood flow, the higher the cardiac output, the faster the speed of blood flow, and vice versa. However, marked variations in blood flow occur in various parts of the vascular system, depending on the cross-section of the vascular bed at any point Thus in a central artery, such as the carotid artery, the flow is very rapid (about 240 mm /sec. in the dog), but only 1 mm./sec. in the capillaries because of the tremendous capillary bed. In the veins, the cross-section decreases, and the speed increases to about 150 mm /sec. in the jugular vein

Because of these marked variations in the speed of blood flow in different vessels, and because there is no simple way of directly measuring the speed of blood flow in man, the circulation time is measured instead. Thus the greater the cardiac output, the shorter the circulation time, and vice versa. However, the circulation time is also related to the circulating blood volume, becoming slower as the blood volume expands, so that if the cardiac output increases, and at the same time the blood volume increases, the circulation time may remain stationary.

One of the mechanisms which produces both the increased heart rate and the increased stroke volume is an increased venous return to the heart With exercise, for example, the flow of blood through the muscles is greatly increased, and an increased amount of blood is massaged out of the veins toward the right heart by the contracting muscles. This muscular activity produces an increased venous pressure, which in turn, causes the heart rate to increase by way of the Bainbridge reflex. (Bainbridge showed in animals that he could make the heart rate increase by an infusion of saline or blood, which increased the venous return and raised the venous pressure. He demonstrated that the heart rate was increased reflexly because it did not appear after section of the vagus and accelerator nerves. Whether the reflex is initiated by the increased venous pressure as Bainbridge believed, or by some other mechanism, is still unknown.)

Exercise further increases the venous return because blood is withdrawn from depots, such as the skin, spleen, *etc* , and the circulating blood volume increases greatly.

3. By increasing the oxygen utilization by the tissues. Normally the arterial oxygen content is 19 volumes per cent (19 cc oxygen in 100 cc arterial blood), and the mixed venous blood coming to the lungs contains about 14 volumes per cent. With severe exercise, the oxygen content of mixed venous blood may decrease to 7 or 8 volumes per cent, and even to 3 or 4 volumes per cent in extreme exercise.

The extent to which these three factors operate to satisfy the oxygen requirements of the body varies in person to person, and even in the same person. For example, in athletes, the resting stroke volume may be 120 to 130 cc , double that of an ordinary person, so that, on exercise, the athlete increases his cardiac output without the great increase in heart rate which occurs ordinarily.

An increase in cardiac output usually results in an increase in the work of the heart, which is the product of the cardiac output and the mean arterial pressure

Measurement of Cardiac Output.—In 1870, Fick showed that the cardiac output could be determined if the oxygen (or the carbon dioxide) content of arterial and mixed venous blood were known, in addition to the total oxygen intake (or carbon dioxide elimination) per minute using the following equation:

$$\underset{\text{(cc per minute)}}{\text{cardiac output}} = \frac{O_2 \text{ intake, cc. per minute}}{\text{art. } O_2\text{, vol.\%} - \text{ven. } O_2\text{, vol.\%}} \times 100$$

Thus, if the oxygen content of arterial blood is 19 volumes per cent, the oxygen content of mixed venous blood is 14 volumes per cent and the oxygen intake per minute is 300 cc , it follows that every 100 cc of mixed venous blood reaches the lungs carrying 14 cc. oxygen, and leaves with 19 cc. Therefore every 100 cc. blood takes up 5 cc. oxygen. Since 300 cc. oxygen are taken up in a minute, this is equivalent to a blood flow through the lungs (from the right ventricle) of:

$$5 \cdot 100 = 300\ X$$

$$X = \frac{30000}{5} = 6000 \text{ cc. or 6 liters per minute.}$$

Arm-to-Lung Circulation Time.—*Ether* gives a good end-point of arm-to-lung circulation time. This is a measure of the time it takes the ether to travel to the right heart and the lungs.

Arm-to-lung time can be measured by injecting 5 minims of ether dissolved in 10 minims of sterile normal saline. The end-point for ether is both subjective and objective, and consists of the patient's perception of the ether vapor in the expired air, which the examiner can also smell. The normal range of the arm-to-lung time is three to eight seconds, with an average of less than six seconds. Instead of ether, 1/4 cc. of paraldehyde can be used, the end-point being a coughing spell. However, side reactions after paraldehyde are common, such as severe cough, narcosis, and local reactions.

Arm-to-tongue and arm-to-lung time determinations can be carried out simultaneously by adding 5 minims of ether directly to the decholin solution.

CIRCULATING BLOOD VOLUME

The total volume of blood in the body consists of the circulating blood volume, that is, the blood which is actually in general circulation, and the reservoir or depot blood volume, which is contained in various organs, such as the liver, spleen, lungs, and skin. This blood is transferred to the general circulation when needed, for example, during exercise, after hemorrhage, *etc.* Marked variations in circulating blood volume may occur in both health and disease, and its measurement may sometimes be valuable for therapy, such as in cases of shock, where the blood volume may fall greatly.

One of the more accurate methods of measuring blood volume is to inject a known quantity (5 cc.) of a dye such as T-1824 (Evans blue) which is eliminated from the blood stream very slowly. After allowing sufficient time for complete mixing of the dye with the plasma (exactly ten minutes), a sample of blood is withdrawn and the concentration of the dye in the sample determined with a photoelectric colorimeter or a spectrophotometer. From the degree of dilution, the circulating plasma volume can be calculated. The circulating blood volume can then be determined from the circulating plasma volume and the hematocrit reading.

Normally, the circulating plasma volume is 40 to 60 cc. per kilogram of body weight, and the circulating blood volume, 70 to 100 cc. per kilogram of body weight.

VENOUS PRESSURE

I pointed out on page 30 that by the time the blood has passed through the arterioles and capillaries and reached the veins, the original, intermittent, forceful, arterial pulsation has given way to a slow, weak, continuous flow back to the right auricle. The venous system can therefore be likened to a system of connecting tubes emptying into a reservoir, the right auricle.

In such a system, the atmospheric pressure causes fluid to mount to the same level in all vessels (water seeks its own level). Thus, in figure 32, the heights of the columns of fluid in tubes *A*, *B*, *C*, vary, but the fluid in all tubes has the same level, relative to the reservoir. This level is known as

the zero level. This lies approximately 5 cm. below the *angle of Louis* (the horizontal ridge which marks the junction between the manubrium and body of the sternum). It represents the upper level of blood in the right atrium and has been called the **central venous pressure.**

A. **Measurement of the Central Venous Pressure.**—Venous pressure can easily be measured in terms of this zero level. For example, let the hand lie limp at the side until the dorsal veins swell, and then gently raise it until the veins just collapse. This should occur about 5 cm. below the angle of Louis. When the venous pressure is elevated, the hand must be raised above this point before the veins collapse This test can be done with the patient lying or standing

The most accurate method of measuring central venous pressure in terms of this zero level would be to measure the actual pressure in the right auricle (atrium) by means of venous catheterization of the heart

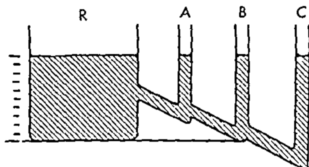


Fig 32 —Diagram showing the mechanics of the venous blood system *A, B, C,* collecting tubes, *R,* reservoir See text

Instead of measuring central venous pressure from the veins of the hand, which is far from the heart, a closer approximation of it can be obtained by measuring the pressure in a superficial vein, like the external jugular vein, which is very near the right auricle Normally, on sitting, no distention of the external jugular or of any of the superficial veins of the neck should be visible When the venous pressure is elevated, the jugular vein may be seen distended even as high as the angle of the jaw, depending on the degree of the increased venous pressure, and the position of the patient.

A fairly exact measurement of the central venous pressure, using the jugular vein, can be made in the following way: The patient should be lying comfortably and relaxed with his head supported on a pillow and all clothing removed from the upper body. The head can be rotated gently in a position to bring out the prominence of the external jugular vein.

The jugular vein should be identified and the point where it collapses marked with a skin marking pencil or with ink It is necessary to be sure that the vein collapses where it seems to, and that it is not merely running deeper in the neck as it ascends To find this out, press a finger on the vein and it will immediately fill and show its whole superficial course.

When the venous pressure is very high, the patient may have to be propped up even to a sitting position Otherwise, the full length of the external jugular vein in the neck may remain distended.

The horizontal level at which the vein collapses is compared to the horizontal level of the angle of Louis (*M* Fig. 33) If the vein collapses at this level, its pressure is + 5 cm of water. (The zero level lies 5 cm below the angle of Louis) If it collapses 2 cm. below this level, its pressure will be + 3 cm of water (5 cm. minus 2 cm. equals 3 cm).

The normal central venous pressure varies from approximately −3 cm. of water to + 8.5 cm. In other words, because of the negative intrathoracic pressure, especially on inspiration, the pressure in the right auricle and in the veins near it may be negative.

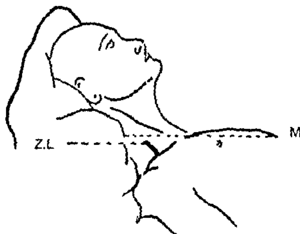


Fig 33 —A method of measuring central venous pressure (after Lewis) *M*, angle of Louis *Z L*, zero level (See text for details)

B. *There is another method of measuring venous pressure. At the surface* of the reservoir, there is only atmospheric pressure, but if one were to go into the depth of the reservoir, the pressure would rise, being directly dependent on the height of the column of fluid above. Thus at the bottom of the reservoir, the pressure is greatest, and is equal to the height of the fluid *in the reservoir plus the atmospheric pressure*

If the reservoir were inaccessible, one could use the height of the fluid in a connecting tube, such as *A*, *B*, or *C*, as an index of the pressure, if one were certain that the base of the tube was at the same level as the base of the reservoir. Thus, in figure 32, the height of tube B is a measure of the *maximum pressure in the reservoir*

Using this concept, venous pressure can be measured manometrically in terms of the pressure which exists at the lowest level of the right auricle. The patient should be lying quietly on his back, in bed, for at least fifteen minutes, because muscular exercise can raise the venous pressure to double *normal values* *The arm is passively and gently raised and supported on a* pillow at about the level of the midaxillary line.

The manometer is a calibrated tube connected by way of a small strip of rubber tubing to an 18 or 20 gauge needle and a 3-way stopcock, and half-filled with a 3 per cent solution of sodium citrate, or with normal saline, to prevent clotting of blood (By using a 3-way stopcock, circulation time studies can also be done along with venous pressure determinations with only one venipuncture.)

The manometer is held vertically and placed so that its zero mark lies 10 cm. above the skin of the back This represents the lowest level of the right auricle (Fig 34) It is about the level of the midaxillary line. An antecubital vein is punctured, and the height at which the citrate solution comes to rest is noted. This is the venous pressure. It normally varies from 20 to 120 mm. of water (This is equivalent to 1.5 to 9 mm. of mercury, because the specific gravity of mercury is 13 6 times heavier than water.)

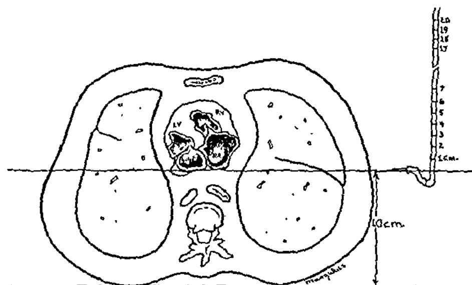


FIG 34.—Diagram showing the position of the manometer used in venous pressure determinations in relation to the lowest level of the right auricle. See text

However, normal values as high as 150 mm. of water have been reported. Values in children are similar to those in adults.

Actually the pressure in an antecubital vein is not identical with the right auricular pressure, because the vein is comparatively far from the right auricle Therefore marked respiratory variations in right auricular pressure, and other cyclic and transient variations may not appear in the antecubital vein.

The Hepato-Jugular Reflux.—When the fluid has reached its maximum level, manual pressure can be applied on the right upper quadrant of the abdomen, over the liver. Normally, the level of the fluid in the manometer remains constant or falls a few millimeters. A rise of 5 mm. or more is abnormal.

The hepato-jugular reflux can be tested without a manometer simply by observing whether the neck veins become swollen as a result of pressure over the liver. The patient should by lying.

The significance of this maneuver, which was first described by W. Pasteur and named the hepato-jugular reflux by French investigators later, is as follows. pressure over the liver forces blood into the inferior vena cava and right auricle. Normally the right auricle dilates to receive this added blood, and no rise in right auricular or venous pressure occurs If right heart failure is present or if the venous pressure is high for any other reason, the blood is forced out into the right auricle, which is already partially distended, and the right auricular and jugular pressures rise.

Factors Affecting Venous Return.—Because of the lack of propulsive force in the veins, there is a tendency for blood to collect and pool in the lower extremities, due to the effect of gravity. Fortunately, there are several factors which help return blood to the heart. The most important of these are the massaging and pumping effect of muscular contractions, especially in the lower extremities and the abdominal wall, and the negative intrathoracic pressure, which helps suck the blood into the heart, especially during inspiration

Venous Pressure in the Lower Extremities.—On lying, the venous pressure in the lower extremities is similar to that in the upper extremities However, on standing, the hydrostatic effect of the column of blood in the veins is added to the venous pressure, so that values as high as 250 mm. of water or more may occur in tall people.

Puncture of the femoral vein can be done to measure the venous pressure in the lower extremities. The vein lies just medial to the femoral artery which can be located just below the inguinal ligament, midway between the anterior superior spine of the ilium and the symphysis pubis Puncture is done about 1 inch below the inguinal ligament, just medial to the pulsation of the femoral artery. The needle is directed upward and inward.

VITAL CAPACITY AND OTHER RESPIRATORY FUNCTION TESTS

The mechanical function of respiration, or ventilation, is concerned with the amount of air that is passed through the lungs per minute of rest or activity (*the breathing requirement*), in relation to the maximum volume of air that can be ventilated per minute (*the maximum breathing capacity*). The *breathing reserve* is the difference between the resting breathing requirement and the maximum breathing capacity It is an important measurement because dyspnea appears whenever the breathing reserve is less than 70 per cent, and sometimes when it is as much as 85 per cent. The average maximum breathing capacity for males is 150 liters per minute, for females, 100 liters. Unfortunately, measurement of the breathing requirement and the maximum breathing capacity requires special spirometers.

The *vital capacity*, on the other hand, is merely the maximum amount of air that can be exhaled after the deepest possible inspiration, and does not have a direct relation to either the breathing requirement or the maximum breathing capacity. Actually it is only a measure of the deepest breath that one can take, and is about 7 times the normal sized breath. However, because it is a simple test to make, it has been widely used

Circulation Time and the Velocity of Blood Flow

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Section 2. The Abnormal Heart

Chapter 7

SYMPTOMS REFERABLE TO THE CARDIOVASCULAR SYSTEM

INTRODUCTION

Most patients come to the cardiologist's office, not to learn that they have mitral stenosis or a calcified aortic valve, but to be relieved of symptoms, such as pain, fatigue, difficulty of breathing, *etc* Such information can be best elicited by means of a careful history It is not within the scope of this book to describe in detail the procedure of history-taking, but several points should be stressed. One of the most important things to do with a new patient is to put him at ease. A frightened patient is a reticent patient who may, willfully or not, conceal important aspects of his condition Suggestions for allaying the patient's initial anxiety, and for uncovering important psychosomatic aspects of the illness are described on page 313

It is a good practice to get answers as specific as possible For example, if the patient complains of pain, direct him to point to the painful area with the tip of the index finger. If his complaint is difficulty in breathing on exertion, determine exactly how much exertion, such as walking, or stair-climbing precipitates the symptoms

Personal habits with respect to smoking, and the imbibition of coffee, tea, the carbonated beverages, such as the "colas" which contain caffeine, are important, because extreme overindulgence may be uncovered in this way

Some of the more important symptoms of heart disease are described below.

PAIN IN THE CHEST

It has been stated that patients who complain of pain in the chest usually do not have heart disease. This is especially true of those patients, especially women, who complain of stabbing or shooting pains in the region of the left nipple. In addition, severe chest pain may also occur in many types of noncardiac disorders Conversely, many forms of serious heart disease, such as cardiac decompensation, complete *a-v* block, subacute bacterial endocarditis, *etc.*, may be present without chest pain. Notwithstanding this, pain is an important symptom of heart disease

Some of the more common types of cardiac and noncardiac conditions which produce chest pain are the following·

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Some of the more common types of cardiac and noncardiac conditions which produce chest pain are the following

Cardiac Conditions.—Angina pectoris (page 294), myocardial infarction (page 593), dissecting aneurism of the aorta (page 659), aneurism of the aorta (page 546), acute pericarditis (page 644), acute rheumatic carditis, neurocirculatory asthenia (page 310), paroxysmal tachycardia (page 341).

Noncardiac Conditions—Subacromial or subdeltoid bursitis, or periarthritis or fibrositis of the left shoulder (page 299), myositis of the pectoral muscles, arthritic or destructive lesions of the cervical or thoracic vertebrae (page 299), slipped rib cartilage (page 299), scalenus anticus syndrome (page 140), herpes zoster (page 299), esophageal diverticulum (page 300), cardiospasm (page 300), hiatus hernia of the stomach (page 299), peptic ulcer (page 300), chronic gall bladder disease (page 300), diaphragmatic flutter (page 300), mediastinal emphysema (page 600), other lesions of the mediastinum, lungs, or pleura

DYSPNEA

Dyspnea or labored breathing, is the sensation of respiratory distress. It thus differs from hyperpnea (page 151) in which an increased depth of respiration occurs without any symptoms of respiratory distress

Dyspnea occurs when the volume of air inhaled per minute (breathing requirement) approaches the maximum volume that the patient can possibly breathe per minute (maximum breathing capacity, see page 111). Dyspnea need not be pathological For example, it can occur in a normal person who performs very strenuous exercise. However, under ordinary circumstances, dyspnea is an abnormal sign, and usually indicates the presence of primary pulmonary disease, obstruction to the upper respiratory tract, or pulmonary congestion due to left-sided heart failure.

Dyspnea can occur in the following ways. by factors causing a marked decrease in maximum breathing capacity, by factors causing an increase in respiratory activity and breathing requirement, or by a combination of both factors

A. Factors Causing a Decrease in Maximum Breathing Capacity.—In cardiac patients, a decreased breathing capacity can occur in the following ways:

1. **Pulmonary Congestion.**—Pulmonary congestion occurs as a result of left-sided heart failure The distended pulmonary vessels encroach on the alveolar spaces, diminishing the breathing capacity of the lungs. In addition, some degree of pulmonary edema or pleural effusion may also be present, further diminishing the effective lung volume.

Pulmonary congestion also interferes with the mechanical aspects of breathing, because the congested lungs become relatively inelastic and rigid This interferes with their expansibility and retractability, and produces a shallow, ineffective type of respiration.

2 Muscular weakness may also be present, due to inadequate oxygenation, and due to the fact that the accessory muscles of respiration, which are utilized by the dyspneic patient, tire easily because they are unaccus-[illegible] to strenuous work

Factors Increasing Respiratory Activity and the Breathing Require-
—The following factors may be present:

1. **The Hering-Breuer Reflex.**—This is stimulated by pulmonary congestion. Normally, respiration is controlled by this reflex. On inspiration, a rise in the tension of the alveoli produces reflex relaxation of the muscles of respiration, and on expiration, the decreased alveolar tension causes stimulation of the respiratory muscles by way of the vagus nerve When pulmonary congestion is present the lungs are rigid and the alveolar tension high, so that the reflex is stimulated with a relatively small intake of air As a result, shallow breathing develops

2. Pulmonary congestion itself can also stimulate the vagus nerve and produce increased respiratory activity (the Churchill-Cope reflex).

3. Increased respiratory activity is also caused by the decreased permeability *of the alveolar walls, due to the pulmonary congestion* As a result of this decreased permeability, the exchange of oxygen, and to a lesser degree, carbon dioxide, is impaired, so that for each liter of air inhaled, less oxygen is absorbed and less carbon dioxide eliminated than normal As a consequence, much more air must be inhaled to attain an adequate uptake of oxygen.

4 During pulmonary congestion the metabolic requirements of the body may rise, requiring increased respiratory effort For example, the basal metabolic rate may rise to + 60 or more during acute left-sided heart failure and the body temperature may rise several degrees

5 Other factors such as tissue anoxia, retention of carbon dioxide in the blood, decreased blood flow through the respiratory center are also of importance

In a patient with left-sided heart failure, dyspnea may be absent at rest, appearing only on exertion (the so-called exertional type of dyspnea) The reason for this is that the increased oxygen consumption demanded with exertion taxes the already poorly functioning respiratory apparatus There is another type of dyspnea that affects cardiac patients, namely paroxysmal nocturnal dyspnea or cardiac asthma (page 236).

When a patient with severe left-sided heart failure develops right-sided heart failure, the dyspnea may decrease in severity, due to the fact that some of the blood, formerly stagnant in the lungs, is now pooled in the liver, the lower extremities and other depots which drain into the right heart

Sighing Dyspnea.—This is a type of functional dyspnea, which should not be confused with true dyspnea Sighing dyspnea occurs as a neurotic symptom in otherwise normal people who complain of being unable to take a deep breath *When told to breathe, they inspire normally. This is followed by a slow*, relaxed expiration accompanied by sighing

ORTHOPNEA

When dyspnea at rest is present, relief from respiratory symptoms can often be obtained by sitting or standing (orthopnea). When the orthopnea is mild, the patient may merely require an extra pillow at night to give him a comfortable sleep When orthopnea is marked, sleep in a sitting position may be required At times, the respiratory distress may be so marked that the patient grasps the side of the bed or a chair, to fix his shoulder girdle and enable him to obtain greater respiratory effort.

Cardiac Conditions.—Angina pectoris (page 294), myocardial infarction (page 593); dissecting aneurism of the aorta (page 659), aneurism of the aorta (page 546), acute pericarditis (page 644); acute rheumatic carditis, neurocirculatory asthenia (page 310); paroxysmal tachycardia (page 341).

Noncardiac Conditions.—Subacromial or subdeltoid bursitis, or periarthritis or fibrositis of the left shoulder (page 299); myositis of the pectoral muscles, arthritic or destructive lesions of the cervical or thoracic vertebrae (page 299), slipped rib cartilage (page 299), scalenus anticus syndrome (page 140); herpes zoster (page 299), esophageal diverticulum (page 300); cardiospasm (page 300), hiatus hernia of the stomach (page 299); peptic ulcer (page 300), chronic gall bladder disease (page 300); diaphragmatic flutter (page 300), mediastinal emphysema (page 600); other lesions of the mediastinum, lungs, or pleura

DYSPNEA

Dyspnea or labored breathing, is the sensation of respiratory distress. It thus differs from hyperpnea (page 151) in which an increased depth of respiration occurs without any symptoms of respiratory distress

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B. Factors Increasing Respiratory Activity and the Breathing Requirement.—The following factors may be present:

nasal drip. Sometimes the cough is worse at night Occasionally it may be paroxysmal, occurring especially after exertion.

The sputum may be mucoid, but may become purulent if secondary infection of the bronchi occur. Streaks or points of blood may be present, and the sputum may show a brownish discoloration, due to hemosiderin, the breakdown product of hemoglobin, which may be free in the sputum, or contained within phagocytic heart failure cells

Heart failure cells are as large or larger than the blood cells Their cytoplasm contains yellow-brown or blackish iron-containing hemosiderin, either in the form of granules or diffusely spread throughout the cell When stained with 10 per cent potassium ferrocyanide and dilute hydrochloric acid, and warmed a little, the iron-containing pigment appears blue These cells are not specific for heart failure, and occur in any case in which there has been pulmonary bleeding of some duration. The heart failure cells should not be confused with black carbon deposits which occur normally

Cough is important because it may be an early symptom, indicating that pulmonary edema is impending This is especially true when cough develops in a patient with paroxysmal tachycardia or acute myocardial infarction.

The presence of cough in a patient with heart disease should not cause one to overlook the fact that the cough may be of noncardiac origin

HEMOPTYSIS

Hemoptysis may or may not occur even in the presence of severe pulmonary engorgement When present, the bleeding may be slight and consist of only streaks or points of blood. With pulmonary edema, a pink, frothy sputum may appear Occasionally massive, frank and sometimes fatal pulmonary hemorrhage may occur, requiring transfusion This occurs in conditions such as mitral stenosis, interauricular septal defects, and the Eisenmenger complex, where marked pulmonary hypertension may be present. Exertion may precipitate the hemoptysis in some cases In others it occurs spontaneously

Pulmonary embolism and infarction is also a cause of pulmonary hemorrhage. Occasionally pulmonary hemorrhage occurs during acute rheumatic fever. The cause of this is uncertain It may be analogous to the epistaxis which occurs, and may be due to a generalized increase in capillary fragility

Hemoptysis occurring in a case of mitral stenosis is due to a strong right ventricle which tends to flood the pulmonary circulation with blood which has difficulty of passing into the left ventricle because of the tight mitral stenosis However, in such cases, acute left-sided heart failure and frank pulmonary edema usually occur instead of hemoptysis. If right-sided heart failure supervenes, the attacks of hemoptysis cease because the pulmonary congestion is lessened. (Dyspnea also decreases for the same reason, page 119)

The occurrence of hemoptysis in a patient with heart disease and pulmonary congestion does not necessarily rule out a noncardiac cause of the hemoptysis. For example, pulmonary tuberculosis occurs not uncommonly in patients with rheumatic and other forms of heart disease

Orthopnea not only occurs with the pulmonary congestion of cardiac origin but can occur whenever the breathing reserve (page 93) is decreased. It therefore may occur in chronic pulmonary disease, mediastinal tumors, and even in cases of marked obesity, in spite of a normal cardiovascular system.

The effectiveness of the sitting or erect position in alleviating orthopnea can be explained as follows.

1. In the erect position, the vital capacity is usually increased, allowing greater pulmonary ventilation.

2. Pulmonary congestion, the cardiac output, and therefore the work of the heart is decreased on standing This occurs because the lower extremities can pool large quantities of blood. This is the reason that some patients with severe orthopnea not only insist on sitting in bed, but keep their feet dangling from the side of the bed.

3 The drainage of the pulmonary veins into the left auricle is such that in the lying position the flow of blood is upward, against gravity, whereas, in the standing position, the flow is downward, thus decreasing pulmonary congestion

4 The erect position may also relieve stasis in the respiratory center of the medulla Thus, it has been found that the dyspneic patient can obtain transient relief by merely flexing the neck. This maneuver does not change the vital capacity but it does raise the level of the medullary center with respect to the right auricle, and facilitates venous drainage from the brain. Similarly, orthopnea occurs in cases of obstruction of the superior vena cava, because of the venous stasis in the medulla.

Trepopnea.—Trepopnea is a form of orthopnea in which the patient experiences respiratory relief by lying in one particular recumbent position, such as the left lateral position rather than the right lateral or horizontal position, *etc*, variations in position probably influencing pulmonary congestion.

COUGH

Cough is usually associated with disease of the respiratory tract, but it commonly occurs in various types of heart disease. The cough may be due to transudation of fluid into the alveoli, but usually is due to congestion of the bronchi Since the bronchial veins empty into the pulmonary veins (which return blood to the left side of the heart) and into the systemic veins (which return blood to the right side of the heart), congestion of the the bronchi and cough may appear with either right-sided or left-sided heart failure. Cough, however, is more common with left-sided heart failure. It may also appear as a result of pulmonary infarction

Occasionally the cough may be the result of mechanical pressure For example, the left bronchus may be displaced by a large left auricle. An aneurism of the aorta may press on the bronchi producing a rasping cough. A dilated pulmonary artery may press on the left recurrent laryngeal nerve, causing hoarseness and a brassy cough. A double aortic arch may compress the trachea.

The cough may be dry, with little or no expectoration, and the patient may have a tickling sensation in the back of his throat, resembling a post-

nasal drip. Sometimes the cough is worse at night. Occasionally it may be paroxysmal, occurring especially after exertion.

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Vertigo, on the other hand is much less common in cardiovascular disease. It may appear in hypertensive cardiovascular disease or cerebral arteriosclerosis if local hemorrhages occur in the labyrinth or related structures

Palpitation.—Palpitation or forceful thumping of the heart is usually due to premature contractions (auricular or ventricular). However, forceful beating of a normal heart may produce palpitation in a nervous person Palpitation may also occur in patients with *a–v* block where the ventricular rate is irregular, and during the course of paroxysmal tachycardia.

Nycturia (Nocturia).—Patients in heart failure frequently are awakened to pass their urine once or more frequently during the night This is known as nycturia. When the nycturia is marked, the total output of urine at night may be greater than that passed during the day. Nycturia is due to the fact that with rest the metabolic needs of the body diminish, so that the cardiac output becomes more nearly adequate Kidney blood flow therefore improves and more urine is formed.

Nycturia of cardiac origin can be differentiated from that due to chronic renal disease by the specific gravity of the urine, because in chronic renal disease the damaged kidneys are unable to concentrate urine even at night and the specific gravity remains 1 012 or lower In such cases, polyuria also occurs during the day. Another common cause of nycturia in the elderly is prostatism.

Fatigue.—Chronic fatigue usually occurs in many noncardiac conditions Occasionally it is an early sign of heart failure

Gastrointestinal Symptoms.—Dyspepsia, anorexia, meteorism, and regurgitation are common findings in patients with chronic heart failure These symptoms may be associated with intense right upper quadrant pain and vomiting due to stretching of the liver capsule when the liver enlarges as a result of right-sided heart failure.

FUNCTIONAL CLASSIFICATION OF PATIENTS WITH HEART DISEASE

The following classification of the New York Heart Association, based both on patient symptomatology and clinical findings, is helpful, especially in surveying large series of cardiac patients:

Functional Capacity

Class I (old classification also I) —Patients with a cardiac disorder without limitation of physical activity Ordinary physical activity causes no discomfort.

Class II (formerly Class II a) —Patients with a cardiac disorder with slight to moderate limitation of physical activity. Ordinary physical activity causes discomfort.

Class III (formerly Class II b).—Patients with a cardiac disorder with moderate limitation of physical activity. Less than ordinary physical activity causes discomfort

Class IV (formerly Class III).—Patients with a cardiac disorder unable to carry on any physical activity without discomfort.

OTHER SYMPTOMS

Hoarseness.—Hoarseness due to paralysis of the left recurrent laryngeal nerve has been observed in cases of mitral stenosis, interauricular septal defects, hypertensive heart disease with congestive failure, aneurisms of the aortic arch, and in noncardiac conditions such as mediastinal tumors, pulmonary tuberculosis, *etc.* It is usually due to compression of the nerve between the dilated pulmonary artery (or the left pulmonary artery) and the inferior surface of the arch of the aorta where the nerve loops around the aorta on its way to the neck. The nerve may also be compressed and incorporated between bands of pericardial and mediastinal adhesions, and may be compressed by enlarged lymph nodes Rarely an aneurism of the arch of the aorta causes hoarseness by compressing the right recurrent laryngeal nerve

The nerve paralysis is accompanied by changes in the voice which becomes hoarse and indistinct, and the patient may not be able to speak above a whisper A characteristic, dry, brassy cough may accompany the hoarseness Laryngoscopic examination reveals either sluggish movement of the left vocal cord, or complete paralysis. Improvement in the cardiac condition may cause the hoarseness to disappear, but if the nerve has been severely injured by pressure, permanent hoarseness may result. It is not known why some patients with a dilated pulmonary artery develop left recurrent laryngeal nerve pressure, and others do not.

Dysphagia.—Dysphagia, or difficulty in swallowing, is a comparatively rare symptom in cardiovascular disease It is due to pressure on the esophagus and has been described in cases of mitral stenosis with a large left auricle, pericarditis with massive effusion, double aortic arch, aneurism of the aorta, and dissecting aneurism of the aorta

Headache and Tinnitus.—A dull, nagging, occipital or vertex headache is a common complaint in patients with hypertension. However, the presence of headache bears no relation to the level of the blood pressure. These hypertensive headaches are probably due to dilatation and distention of certain branches of the external carotid artery. There is also a large pychological element present The headache of hypertensive encephalopathy is due to increased intracranial pressure

Hypertensive patients also often complain of a continuous or intermittent buzzing noise in the ear (tinnitus), possibly due to the flow of blood through a tortuous arteriosclerotic artery near the middle ear. However, why the tinnitus should appear and disappear is unknown.

Vertigo and Dizziness.—In vertigo, there is a sensation that the outer world is revolving about a person (objective vertigo), or that the person himself is moving in space (subjective vertigo). Dizziness or giddiness, on the other hand, consists in an abnormal sensation of unsteadiness, characterized by a feeling of movement within the head, but there is no sensation that either the external world or the patient is in motion.

Dizziness often occurs in patients with hypertensive cardiovascular disease, or cerebral arteriosclerosis, but may occur in cases of petit or grand mal, cerebral neoplasms or abscesses, and in psychoneurotic persons. In my experience it seems to be precipitated especially by emotional tension in hypertensive patients.

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Therapeutic Classification

Class A.—Patients with a cardiac disorder whose ordinary physical activity needs no restriction

Class B.—Patients with a cardiac disorder whose ordinary physical activity needs no restriction but who should be advised against unusually severe or competitive efforts

Class C.—Patients with a cardiac disorder whose ordinary physical activity should be moderately restricted, and whose more strenuous habitual efforts should be discontinued

Class D.—Patients with a cardiac disorder whose ordinary physical activity should be markedly restricted.

Class E—Patients with a cardiac disorder who should be at complete rest or confined to bed.

No Heart Disease. Predisposing Etiological Factor (formerly Potential Heart Disease).—These are patients in whom no heart disease is discovered, but whose course should be followed by periodic examinations because of the presence or history of an etiological factor that might cause heart disease

Undiagnosed Manifestation (formerly Possible Heart Disease)—Patients with symptoms or signs referable to the heart but in whom a diagnosis of heart disease is uncertain

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See references under Angina Pectoris (p 307), and Myocardial Infarction (p 608)

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Chapter 8

ABNORMAL PHYSICAL SIGNS REFERABLE TO THE CARDIOVASCULAR SYSTEM

INTRODUCTION

When heart disease is present, physical examination may or may not reveal abnormal physical signs For example, in a patient with angina pectoris and a healed myocardial infarct, the findings on physical examination may be completely "normal," diagnosis being made from the history and electrocardiographic findings, and even the electrocardiogram may have returned to normal

When heart disease is present along with abnormal physical signs, the abnormal signs are not confined to the chest, and it is a wise cardiologist who does a complete physical examination on each of his patients. For purposes of simplification, some of the more important abnormal physical signs referable to the cardiovascular system shall be described under several arbitrary headings:

THE GENERAL APPEARANCE OF THE PATIENT

Even superficial observation of a patient may provide valuable clues as to the diagnosis For example, the child who lies in a knee-chest position or sits with his chest bent far forward has probably a large pericardial effusion A yellowish "washed-out" appearance in a young person is suggestive of subacute bacterial endocarditis The plethoric countenance of a patient who complains of headache may lead to a diagnosis of polycythemia vera Edema, cyanosis, jaundice, and pallor are also valuable general signs, which can be considered in more detail Fever is discussed on pages 46 and 241.

EDEMA

Edema can be defined as an accumulation of sufficient fluid in the extracellular tissue spaces to produce physical signs. In other words, the term edema applies to a gross accumulation of fluid For example, the volume of a lower extremity may increase 8 per cent before physical evidence of edema, such as pitting of the skin on pressure occurs. For practical purposes it can be assumed that this excess fluid is derived solely from the blood plasma, neglecting the fact that the cells of the body contain about 50 per cent of the total fluid in the body and are capable of causing changes in the extracellular (interstitial) fluid.

Edema may be localized to the subcutaneous tissues of the lower extremities or other dependent regions, or it may be generalized, in which case it

is called anasarca. The old terms, dropsy, and hydrops, were applied both to edema as defined above, and to free collections of fluid in the pleural cavity (hydrothorax or pleural effusion) or the abdomen (ascites). Edema of the organs, such as the lung, brain, liver, *etc.* may also occur.

Actually it is not the retention of fluid or water as such that causes the edema but rather the retention of the crystalloid electrolytes, dissolved in the water, the most important of which are the sodium and chloride ions The reason for this becomes obvious when one examines the normal composition of electrolytes in the plasma and tissue fluids.

The average normal electrolyte content of plasma and of interstitial fluid, in terms of milliequivalents per liter is as follows:

Cations	*Plasma*	*Interstitial fluid*
Na	142	145
K	4 5	4
Ca	5	2 5
Mg	3	2
anions		
Cl	103	114
HPO_4	2	2
HCO_3	27	30
SO_4	1	1
Organic acid	2	2
Protein	16	1

In other words, edema is produced by the retention of salt and water in the tissue spaces

How Does Salt and Water Escape From the Blood Stream and Accumulate in the Tissue Spaces?– The interaction of the following factors determines whether or not salt and water remain in the blood vessels Here again, for practical reasons, it will be assumed that the exchange of fluids occurs *solely in the capillaries.*

1. **The Capillary Blood Pressure (Hydrostatic Pressure)** —This tends to force fluid into the tissue spaces Normally at the arterial end of the capillaries the blood pressure is 32 mm mercury, but at the venous end, the pressure has dropped to 12 mm Thus, fluid which has been forced out at the *arterial end of the capillaries will tend to return at the venous end, because* of the lowered blood pressure there

2. **The Colloid Osmotic (Oncotic) Pressure of the Plasma Proteins.**—This tends to hold fluid in the capillaries Osmotic pressure depends on the presence of two solutions separated by a membrane which is permeable to some but not all of the substances dissolved in the solutions Such a membrane is called semi-permeable The capillary walls act as a semi-permeable membrane, being freely permeable to the crystalloid electrolytes, but almost completely impermeable to the plasma proteins A much higher concentration of proteins is therefore present in the bloodstream than in the tissue spaces, and the osmotic pressure thus produced in the capillaries tends to draw water into the blood vessels Since the osmotic pressure of a substance is *proportional to the number of molecules in solution,* the albumin fraction of the plasma proteins causes the major part of the osmotic pressure, first, because, normally, albumin constitutes most of the blood protein, and secondly, its molecular weight is much smaller than that of the

globulin This is also the reason that a concentrated solution has a greater osmotic pressure than a dilute solution. The osmotic pressure of the plasma proteins at the arterial end of the capillaries is 25 mm, almost equal to the hydrostatic force of the capillary blood pressure. At the venous end, the osmotic pressure rises, because the plasma is more concentrated This tends to redraw fluid into the vessels

3 **The Colloid Osmotic (Oncotic) Pressure of the Proteins in the Tissue Spaces.**—This tends to hold fluid in the tissue spaces. Some protein is present in the tissue spaces because the capillaries are not completely permeable to protein and about 0 5 per cent protein leaks into the tissue spaces However, the osmotic pressure of this small quantity of protein is negligible (less than 2 mm)

4 **Tissue Pressure.**- Tissue pressure is the pressure or force with which the tissues resist distention or displacement by fluid. Tissue pressure tends to force fluids into the blood vessels The tissue pressure averages 2 8 mm. mercury but varies greatly in different parts of the body In the loose areolar tissue under the eyes, it is very small Under the tense skin of the pretibial area it is quite high.

The resultant effect of all these factors on the fluid exchange between capillaries and tissue spaces can be summarized as follows: At the arterial side of the capillaries, the blood pressure is greater than the plasma osmotic pressure and the tissue pressure combined, and salt and water escape into the tissue spaces At the venous end of the capillaries, the blood pressure has dropped below the combined values of the osmotic pressure which has risen because the plasma is more concentrated, and of the tissue pressure which has also risen, because of the fluid which has entered. Salt and water therefore re-enter the capillaries

From this, one can deduce that an increased capillary blood pressure, a decreased plasma osmotic pressure, and a decreased tissue pressure all favor filtration of salt and water out of the blood vessels and the production of edema; and a decreased capillary blood pressure, an increased capillary osmotic pressure, and an increased tissue pressure favor reabsorption of the salt and water. Normally there is approximate balance between these factors, and excess fluid and salt and most of the protein which remain in the tissue spaces are carried back to the systemic circulation by way of the lymphatics.

None of these factors alone is ordinarily capable of producing edema. For example, on standing, the venous pressure at the ankles of a normal person reaches several hundred millimeters of water, yet edema does not occur *This is due to the fact that as fast as fluid is forced out of the capillaries*, the pumping action of the muscles, and the increased tissue pressure force it back into the systemic circulation. Similarly, ligation of the inferior vena cava in a normal person causes the venous pressure in the lower extremities to rise to 600 cm or more of water, yet edema need not occur. (One reason for this is that the blood is carried back into the heart by way of collateral vessels In addition, the lymphatic drainage becomes markedly increased.) However, increased venous pressure plays an important role in the production of edema, because local rises in venous pressure determine where the edema is to appear. This occurs in the following way:

One of the primary events that happens in cardiac decompensation is a reduction of the cardiac output (either below normal or below the previous level for that person) This produces a marked decrease in the blood flow through the kidneys, possibly as a compensatory means of counteracting the decrease in cardiac output because normally as much as one-fifth of the cardiac output goes to supply the kidneys. Thus, a decreased kidney blood flow allows blood to be directed to more vital organs

As a result of the decreased kidney blood flow, glomerular filtration of salt and water and other substances is decreased one-third or more. When one remembers that normally 99 5 per cent of the filtered salt is reabsorbed by the tubules and conserved in the body, and that only about 0 5 per cent is excreted, it is easy to understand that when filtration is cut one-third, the tubules receive so much less salt than they are accustomed to handle that they reabsorb practically all the salt in the glomerular filtrate, leaving practically nothing for excretion in the urine. (Even such powerful diuretics as the parenteral mercurial preparations rarely reduce tubular salt reabsorption below 96 per cent.)

An even more important factor in the development of edema is that when heart failure occurs, the reabsorptive capacity of the renal tubules for sodium becomes abnormally increased.

Since salt can only be retained in an isotonic solution, the net result of the retention of salt in the body is to increase the total plasma volume. Since the capacity for fluids in the venous system is limited, this results in a dilatation of the veins, an increase in venous pressure, and a decrease in osmotic pressure, because of dilution of the blood, and finally, edema, depending on where the venous pressure is highest. The dilution of the blood proteins stimulates further protein formation so that eventually the blood protein level tends to return to normal

There is another mechanism responsible for the retention of sodium, namely, the presence within the brain of "volume receptors," which respond to changes in the volume of intracranial, extracellular fluid For example, in normal people, erect posture, such as quiet standing or sitting causes a reduction of renal sodium excretion as compared with the sodium excretion in the recumbent or head-down position. (However, these postural effects are unexplainably absent in cases of heart failure.)

Hormonal and other factors in edema formation are discussed on page 233

Local factors affecting venous pressure determine where the edema will appear. In an ambulatory patient with cardiac decompensation, dependent edema appears around the ankles or in the pretibial area, disappearing after a night's rest in bed This can be recognized by gentle pressure with the thumb over the lower tibia The edema fluid is displaced, leaving an indented, pitted area which remains for a few minutes.

If the patient lies on his back a good part of the day, edema of the legs may be minimal or absent, but presacral edema may occur. Also, if the tissue pressure of the lower extremities is high, the skin being taut, edema is less likely to appear here than in other locations. In markedly orthopneic patients, the lower extremities, the genital regions and even the abdominal wall may be markedly edematous.

globulin. This is also the reason that a concentrated solution has a greater osmotic pressure than a dilute solution. The osmotic pressure of the plasma proteins at the arterial end of the capillaries is 25 mm., almost equal to the hydrostatic force of the capillary blood pressure. At the venous end, the *osmotic pressure rises, because the plasma is more concentrated.* This tends to redraw fluid into the vessels.

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4. **Tissue Pressure.**—Tissue pressure is the pressure or force with which the tissues resist distention or displacement by fluid. Tissue pressure tends to force fluids into the blood vessels. The tissue pressure averages 2.8 mm. mercury but varies greatly in different parts of the body. In the loose areolar tissue under the eyes, it is very small. Under the tense skin of the pretibial area it is quite high.

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characteristically dry and wrinkled. The edema of varicose veins has already been mentioned. Obstruction of the superior vena cava may result in localized edema and cyanosis of the face and upper extremities (page 672) Obstruction of the inferior vena cava may result in localized massive edema of the lower extremities, the genitalia, abdominal wall and back (page 675). Local conditions causing edema, such as cellulitis, angioneurotic edema, *etc.*, need not be considered here.

CYANOSIS

Cyanosis is the diffuse, dusky, bluish color of the skin and mucous membranes produced by the presence of an increased quantity of reduced hemoglobin in the superficial capillaries. Cyanosis is directly related to the amount of reduced hemoglobin in the blood, or more exactly, to the amount of reduced hemoglobin in the superficial capillaries, and occurs only when there is 5 grams or more reduced hemoglobin per 100 cc. of capillary blood. This is equivalent to a 6 5 volume per cent oxygen unsaturation of the capillary blood because 1 gram of reduced hemoglobin can combine with 1.34 cc. of oxygen. (The oxygen unsaturation of blood can be determined by first drawing blood under oil and determining the quantity of oxygen combined with hemoglobin. Then a sample of blood is drawn, aerated, and the total oxygen content is determined The difference between these two values, making allowance for the oxygen dissolved in the plasma, is the oxygen unsaturation.)

Normally, there is as much as 15 grams of hemoglobin per 100 cc. of blood Since 1 gram of hemoglobin can combine with 1.34 cc. of oxygen, 15 grams of hemoglobin are able to carry 20 cc of oxygen. In other words, the *oxygen capacity* of blood with 15 grams of available hemoglobin per 100 cc. is 20 volumes per cent. Since only 94 to 97 per cent of the hemoglobin in arterial blood is combined with oxygen, the *oxygen content* of arterial blood is approximately 19 volumes per cent, and the *oxygen unsaturation* of arterial blood is approximately 1 volume per cent

In the passage of the blood to the veins, oxygen is given off to the tissues, so that the oxygen content in venous blood is about 14 to 15 volumes per cent, and the venous oxygen unsaturation 5 to 6 volumes per cent. This produces the bluish color of venous blood

However, the cyanosis of the skin is produced by reduced hemoglobin and oxygen unsaturation in the capillaries and not in the veins. The capillary oxygen unsaturation is roughly the average of that of the arteries and veins Thus, using the above values, capillary oxygen unsaturation would be $\frac{1+5}{2} = 3$ volumes per cent. No cyanosis occurs under these conditions because as was mentioned above, cyanosis requires an oxygen unsaturation of about 6 5 volumes per cent

A high red blood count facilitates the production of cyanosis, a low blood count tends to prevent it For example, in a normal person with 15 grams of hemoglobin per 100 cc blood, about one-third of the hemoglobin must be reduced before cyanosis occurs. However, in polycythemia, with 20 grams of hemoglobin, only about one-fourth of the hemoglobin need be

The presence of varicose veins may cause edema to appear first on the lower extremity with the varices. In this connection it can be mentioned that the most common cause of unilateral or bilateral edema of the lower extremities is the presence of varicose veins, and not heart disease. Marked pulmonary edema may occur with little edema elsewhere if increased pulmonary venous and capillary pressure result from a transient decrease in the output of the left ventricle, the right ventricular output remaining unchanged (see page 234).

Cardiac edema has been contrasted with nephritic and nephrotic edema because cardiac edema rarely occurs on the face and eyelids, being mostly dependent in distribution The reason for this is that most patients with severe cardiac edema are orthopneic, and the edema fluid gravitates downward, whereas in renal disease, the patients frequently sleep flat in bed Changes in capillary permeability, due to anoxemia or other factors, are probably not important in either cardiac or renal edema, because the protein content of the edema fluid in either case is low and similar to normal interstitial fluid, about 0.5 per cent, contrary to what would occur if the capillary permeability were increased.

In acute nephritis or in the nephrotic syndrome, the injured glomeruli are unable to function As a result, the effective renal blood flow is decreased (This is similar to what happens in heart failure) In addition, there is evidence that the renal tubules reabsorb more than normal quantities of sodium, which causes sodium retention.

Both cardiac and renal edema are soft and pit on pressure. Renal edema may be softer than cardiac edema probably because it is usually more marked (the low plasma protein level of renal disease tends to aggravate the edema). The edematous limbs have a pale, shiny, white appearance and become wrinkled as the fluid disappears.

When edema occurs as a result of lymphatic obstruction, the protein which escapes from the capillaries is unable to return to the systemic circulation, and such edema fluid has a high protein content The accumulation of protein in the edema fluid results in fibrin formation and interstitial fibrosis, and an indurated non-pitting edema results, unlike the usual soft, pitting edema of cardiac and renal origin However, when cardiac edema persists for any length of time, thickening of the skin and induration may occur as a result of the proliferation of collagenous fibers, and the skin assumes a rough, brawny, reddened and pigmented appearance, similar to that seen with lymphatic obstruction. Rarely, the edematous skin may crack or rupture, resulting in drainage of the edema fluid, which may persist for some time. Such a region is very susceptible to infection and should be treated with sterile precautions.

Cardiac edema can also be differentiated from edema due to lymphatic obstruction by *determining the cholesterol content of the edema fluid.* It is low in cardiac edema, averaging about 15 mg. per cent, and high in edema due to lymphatic obstruction, averaging about 175 mg. per cent. The edema fluid can be obtained for analysis by inserting an 18 gauge needle subcutaneously and letting the fluid drip into a test tube.

Noncardiac causes of edema should always be kept in mind. For example, in myxedema, a non-pitting edematous infiltration appears, and the skin is

characteristically dry and wrinkled. The edema of varicose veins has already been mentioned. Obstruction of the superior vena cava may result in localized edema and cyanosis of the face and upper extremities (page 672). Obstruction of the inferior vena cava may result in localized massive edema of the lower extremities, the genitalia, abdominal wall and back (page 675) Local conditions causing edema, such as cellulitis, angioneurotic edema, *etc.*, need not be considered here.

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Normally, there is as much as 15 grams of hemoglobin per 100 cc. of blood. Since 1 gram of hemoglobin can combine with 1 34 cc. of oxygen, 15 grams of hemoglobin are able to carry 20 cc of oxygen. In other words, the *oxygen capacity* of blood with 15 grams of available hemoglobin per 100 cc is 20 volumes per cent. Since only 94 to 97 per cent of the hemoglobin in arterial blood is combined with oxygen, the *oxygen content* of arterial blood is approximately 19 volumes per cent, and the *oxygen unsaturation* of arterial blood is approximately 1 volume per cent.

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A high red blood count facilitates the production of cyanosis; a low blood count tends to prevent it For example, in a normal person with 15 grams of hemoglobin per 100 cc. blood, about one-third of the hemoglobin must be reduced before cyanosis occurs. However, in polycythemia, with 20 grams of hemoglobin, only about one-fourth of the hemoglobin need be

reduced to cause cyanosis. This occurs easily because of the sluggish blood flow usually present in polycythemia. Conversely, in a patient with severe anemia, cyanosis rarely occurs, even if all the conditions necessary for it are present

Cyanosis can be produced by increasing arterial oxygen unsaturation (*central cyanosis*), or by increasing the utilization of oxygen by the tissues, thus increasing the venous oxygen unsaturation (*peripheral cyanosis*), or by a combination of both factors (*mixed cyanosis*)

Central Cyanosis.—If arterial blood has an increased oxygen unsaturation of 4.5 volumes per cent, instead of a normal 1 volume per cent unsaturation, and if the tissues extract the usual 5 volumes per cent of oxygen, the capillary blood will have an oxygen unsaturation of $\frac{4.5 + 9.5}{2} = 7$ volumes per cent, and cyanosis will appear In a case of central cyanosis, such as this, notice that the arterio-venous oxygen difference remains the same as normal (5 volumes per cent)

Arterial oxygen unsaturation can increase in the following ways.

1 **Venous-arterial Shunts**—In congenital lesions such as septal defects, or an overriding aorta, etc., it has been determined that when about one-quarter or more of the blood from the right ventricle is shunted into the systemic circulation, cyanosis occurs As a general rule, the greater the shunt, the more intense the cyanosis will be

In cases of congenital heart disease with septal defects and cyanosis, as in the tetralogy of Fallot, the volume of blood flowing into the lungs is very small In such cases, it had been assumed in the past that this was the cause of the cyanosis. The reasoning for this was that even if all the blood flowing into the lungs were completely oxygenated, there would still be sufficient unoxygenated blood flowing through the body to produce cyanosis This assumption is wrong, because in cases of pure pulmonary stenosis with intact septa, cyanosis does not develop, even though the blood flow through the lungs is very inadequate.

2. **Failure of the Blood to Be Fully Oxygenated in Its Passage Through the Lungs.**—It is a well-known fact that lowered barometric pressure produces low oxygen tension in the pulmonary alveoli and incomplete saturation of the arterial blood. As a result, cyanosis can occur in an otherwise normal person who is living at a high altitude, especially above 10,000 feet elevation

The most important pathological condition in which blood cannot be completely saturated in its passage through the lungs is in *chronic pulmonary emphysema*, and less frequently in cases of *pulmonary fibrosis*. The cyanosis which is often seen in patients with severe left-sided heart failure and pulmonary congestion is due to stagnation of blood in the extremities and is therefore a peripheral cyanosis (see below) rather than a central cyanosis. There is no proof even in severe left-sided failure that the blood leaving the lungs is incompletely saturated with oxygen.

Emphysema produces cyanosis because of the presence of loss of elasticity of the lungs and poor pulmonary ventilation *Pulmonary fibrosis* is also associated with poor pulmonary ventilation In addition, in rare cases, there may be actual thickening of the alveolar membrane (as in

acute *interstitial fibrosis* and in *beryllium poisoning*) which interferes with the exchange of oxygen in the lungs.

Central cyanosis will not occur in patients with pulmonary hypertension, such as occurs in Ayerza's syndrome (page 636) unless pulmonary emphysema or fibrosis is also present

Peripheral Cyanosis.—If the arterial oxygen unsaturation remains normal, about 1 volume per cent, but the tissues utilize more oxygen because of stasis or other reasons the venous oxygen unsaturation may rise to 13 volumes per cent or more. In such a case, the capillary unsaturation would be $\frac{1 + 13}{2} = 7$ volumes per cent, and cyanosis appears. In cyanosis of the peripheral type, as in this case, notice that the arterio-venous oxygen difference is much greater than normal (12 volumes per cent instead of 5)

Increased tissue utilization of oxygen can cause increased venous oxygen unsaturation and cyanosis in the following ways:

1 The peripheral circulation can be slowed by cold, excess vasomotor stimulation, *etc.* The slow circulation allows more oxygen to be withdrawn from the blood by the tissues and cyanosis occurs. This frequently is associated with capillary dilatation, which makes the cyanosis more obvious. Capillary dilatation is increased when carbon dioxide accumulates in the blood, so that when oxygen deficiency is associated with carbon dioxide accumulation, as in obstruction to the trachea, emphysema, or venous congestion to a superficial region, cyanosis may be intense.

2. Increased venous pressure may produce slowing of the blood, stagnation and cyanosis as in cases of right-sided heart failure, tricuspid stenosis, acute, or chronic constrictive pericarditis, or in any condition which locally increases the venous pressure, such as venous thrombosis, a tourniquet around a limb, *etc*

3 In shock, cyanosis may occur as a result of marked vasomotor collapse and stagnation of blood.

Differentiation of Peripheral from Central Cyanosis—*Peripheral cyanosis* is usually due to stagnation of blood and it will therefore occur in dependent and peripheral regions, such as the limbs and the face These are characteristically cold.

Central cyanosis, on the other hand, is a generalized cyanosis and it affects not only the skin of the face and hands but the mucous membranes, even within the mouth, and the skin of the trunk However, the trunk rarely shows cyanosis because there is usually not enough blood in the skin there. In addition, and more important, the skin showing the central type of cyanosis will be warm or hot

Thus, if one suspects a central cyanosis in a skin which is cool or cold, the skin should be warmed by massage or heat If the cyanosis is peripheral, it will disappear when the skin becomes warm A central cyanosis will persist.

Mixed Cyanosis.—A case of cyanosis may have some degree of central and peripheral factors Thus, in cor pulmonale due to pulmonary emphysema or pulmonary fibrosis, the emphysema or fibrosis will tend to produce a central type of cyanosis, whereas if right-sided heart failure is also present, the peripheral type of cyanosis will tend to appear.

Clinical Aspects of Cyanosis.—The depth of cyanosis locally varies with the state of the cutaneous capillaries and the pigmentation and thickness of the skin. Cyanosis can best be observed in peripheral areas such as the feet and hands, where the skin is thin and unpigmented and the capillaries numerous, as in the cheeks, ears, lips, nail beds, and in the mucous membranes of the mouth, but not in the conjunctiva or sclera.

There is no strict correlation between the degree of arterial oxygen saturation and the presence of cyanosis. In one patient, cyanosis may develop when the arterial oxygen saturation falls to 80 per cent, in another patient, cyanosis will not appear until the arterial oxygen saturation falls to 60 per cent

When the skin temperature drops below 50 to 55° F. (10 to 15° C.), the hemoglobin is able to give up very little oxygen As a result, the skin remains red instead of developing the purple hue of cyanosis, even though the conditions necessary for cyanosis are present This is sometimes seen in patients in shock

The two common causes of central cyanosis are congenital heart disease with a venous-arterial shunt, and chronic pulmonary disease. These can be differentiated by the arterial carbon dioxide content The normal carbon dioxide arterial content varies from 44 to 52 volumes per cent. In *congenital heart disease with cyanosis, the arterial carbon dioxide content* is less than 44 volumes per cent, because there is no disturbance with the mechanical aspects of pulmonary ventilation and hyperventilation occurs to compensate for the cyanosis. This reduces the arterial carbon dioxide content below normal. However, chronic pulmonary disease with cyanosis is due to a disturbance of pulmonary ventilation. As a result, the arterial carbon dioxide content is usually above 52 volumes per cent when cyanosis is present

When cyanosis is associated with shock, the skin has a blue-gray, leaden hue, due to the poor filling of the capillaries If the red blood count is high, the cyanosis may have a reddish hue. In this connection, one should not forget that while cyanosis may occur in polycythemia vera, it is more common to find a secondary polycythemia which has resulted from the cyanotic condition The differences between polycythemia vera and secondary polycythemia are described on page 727

A cyanotic tint to the cheeks, the malar flush, is common in mitral stenosis, but it has been reported in myxedema, and may be simulated by the dilated cheek capillaries of some normal people, and of patients with cirrhosis of the liver. When cyanosis is present with jaundice, the skin appears bluish-yellow, and the scleras become icteric but not cyanotic.

Congenital heart disease should always be suspected when cyanosis is associated with clubbing of the fingers, and with polycythemia. In such cases, the cyanosis precedes the clubbing. When congenital heart disease is present and the cyanosis dates from birth or early infancy, tetralogy of Fallot, transposition of the great vessels, truncus arteriosus, aortic atresia, undeveloped right ventricle with tricuspid atresia can be suspected Cyanosis may develop late in childhood, adolescence or adulthood in congenital lesions such as pulmonary stenosis, interauricular septal defects, isolated interventricular septal defects, and the Eisenmenger complex.

Localized cyanosis of the body above the brim of the pelvis occurs with transposition of the great vessels, associated with a patent ductus arteriosus.

Localized cyanosis below the brim of the pelvis occurs with an absent aortic arch with a patent ductus arteriosus, an infantile coarctation of the aorta with a patent ductus arteriosus, or a patent ductus arteriosus with pulmonary hypertension and a right to left shunt through the ductus.

The best way to judge such local cyanosis in an infant is to place the hand next to the foot.

Methemoglobinemia.—Methemoglobinemia and sulfemoglobinemia, produced by the ingestion of aniline derivatives, nitrates, and other drugs, cause a discoloration of the skin that resembles cyanosis However, in such cases, there is no abnormality of the heart, and polycythemia is absent. Diagnosis is made by examination of a sample of the patient's diluted blood with a pocket spectroscope. Characteristic absorption bands will appear

Recently methemoglobinemia has been described in infants under ten weeks old living in rural communities. The methemoglobinemia develops when well water, containing an excess of nitrates is used in the preparation of the formula. (10 parts per million is considered a safe upper limit.)

The cyanotic-like discoloration of the skin disappears within thirty-six hours after the water supply is changed, and no other treatment is ordinarily needed However, if the baby appears critically ill because of the lack of available oxyhemoglobin, methylene blue can be given intravenously in a dose of 1 mg per kg of body weight. Thus, 0 5 cc of a 1 per cent solution of methylene blue would be sufficient for an eight pound infant. Ascorbic acid, 100 mg intramuscularly, can also be used.

JAUNDICE

Because of the marked congestion of the liver which occurs with chronic right-sided heart failure, liver function tests, such as the bromsulfalein test, cephalin flocculation reaction, *etc* , become abnormal, and the bilirubin content of the blood may increase With the increased bilirubin in the blood, faint or mild jaundice may appear Jaundice may also be precipitated in cases of heart failure by pulmonary infarction. It appears suddenly from two to four days after the infarct. In the absence of heart failure, pulmonary infarction rarely if ever causes jaundice.

The mechanism by which jaundice occurs in heart disease can be briefly explained as follows. Normally the hemoglobin of broken-down red blood cells is converted into bilirubinogen (bilirubin combined with a protein, globin) (indirect-reacting bilirubin) by the reticulo-endothelial cells of the bone marrow, the spleen and the Kupffer cells of the liver Bilirubinogen is absorbed into the bile canaliculi of the liver, converted to sodium bilirubin (free, or direct-reacting bilirubin) and excreted with the bile into the colon where it is converted to urobilinogen, most of which is excreted in the feces (where it is oxidized to urobilin) and part of which is reabsorbed into the systemic circulation and excreted by the kidneys in the urine

In determining the bilirubin content of the serum, the old qualitative Van den Bergh test has been adapted for quantitative measurements of

serum bilirubin by Malloy and Evelyn. When this method is used and serum is mixed with the diazo reagent, the red color that develops within a minute is a measure of the amount of free bilirubin present. It is similar to the old direct Van den Bergh reaction. When serum is mixed with 50 per cent methyl alcohol in addition to the diazo reagent, the color that develops in fifteen minutes is a measure of the total bilirubin, that is, the free bilirubin, plus bilirubinogen and the difference between them measures the amount of bilirubinogen or indirect-reacting bilirubin present. Normally, no free bilirubin is present, and less than 0.5 mg. per cent bilirubinogen. Abnormalities of this process can produce two types of jaundice, *retention jaundice*, and *regurgitation jaundice*.

Retention Jaundice.—The liver cells are unable to remove all the bilirubinogen from the blood, where it is retained. When sufficient bilirubinogen accumulates, jaundice appears. Such jaundice is associated with a delayed serum bilirubin test, and an increased amount of urobilinogen in the urine. (Normally, up to 8 mg. urobilinogen per 100 cc. urine is present.) The stools are not decolorized.

Heart failure can cause retention jaundice in two ways: (*a*) congestion of the liver produces anoxia of the cells which become unable to transform bilirubinogen completely. (*b*) the heart failure cells of the lung and the reticulo-endothelial cells in other parts of the body may break down a sufficient excess of hemoglobin from stagnated red cells to overburden the subnormally functioning liver with more bilirubinogen than it can convert. Pulmonary embolism can aggravate this process, not only because of the increased blood destruction in the infarcted area of the lungs, but also because the infarct intensifies the anoxia of the liver.

Regurgitation Jaundice.—When necrosis of some of the liver cells occurs, bilirubinogen passes through the normal cells and is converted to free bilirubin in the usual way, but a large portion of the free bilirubin regurgitates around and through the necrotic cells and enters the tissue spaces and is absorbed into the systemic circulation. This factor is a cause of jaundice in cases of chronic right-sided heart failure where marked congestion of the central veins of the liver lobules occurs, with atrophy and even focal hemorrhage and necrosis of the neighboring cells.

When regurgitation jaundice develops, direct-reacting bilirubin is present in the blood, and the urine may contain bilirubin. However, the stools are not decolorized. Most cases of cardiac jaundice have both retention and regurgitation elements.

When jaundice develops in an edematous patient, the jaundice is not visible in the edematous areas. Apparently the diffusion of the large bilirubin molecule through edematous fluid is a slow and difficult process. However, jaundice and cyanosis can coexist in the skin.

The occurrence of cardiac jaundice is a serious sign, but the jaundice will gradually disappear as cardiac compensation is restored. It should be remembered however, that even in a cardiac, the jaundice may be due to noncardiac causes.

PALLOR

Pallor is usually associated with anemia. In an adult, persistent pallor, especially if the skin has a yellow subicteric tint, suggests subacute bacterial

endocarditis. In children, pallor and anemia are common signs of rheumatic activity. Acute and chronic nephritis can also cause pallor. However, pallor without anemia is common even in noncardiac patients confined indoors for any length of time, and of course can occur in any case of acute or chronic anemia regardless of etiology. In this connection, one should remember that severe anemia can produce marked cardiovascular disturbances, such as dilatation of the heart, murmurs, and severe heart failure

VARIATIONS IN BODY WEIGHT

For patients with heart failure, the scale is more important than the stethoscope A sudden gain of several pounds in weight may be the first indication that the patient's compensation is failing, and a gain in weight is an excellent guide for the use of the mercurial diuretics (see page 247) In this connection, one should remember that when a patient in severe failure is treated properly, his appetite may improve so that over a long period he may gain weight due to improved nutrition

In children with rheumatic fever, a failure to gain weight is a presumptive sign that rheumatic activity is still present.

ABNORMAL PHYSICAL FINDINGS IN THE EXTREMITIES

Clubbed Fingers.—Clubbing consists of enlargement of the soft parts of the terminal phalanges with longitudinal and transverse overcurving of of the nails The diagnosis of marked clubbing presents no difficulty, but when minimal, it may be overlooked, and the following signs are valuable in detecting it.

1. The soft tissues at the base of the nail develop a spongy feel on pressure, and the nail base seems to be floating.
2. The skin over the base of the nail develops a taut, shiny appearance.
3. The normal angulation between the nail base and the skin fold disappears, and a convexity occurs (Fig. 35)

Clubbing occurs characteristically in congenital heart disease with venous-arterial shunts, in association with cyanosis If clubbing is present without cyanosis, congenital heart disease is probably not the cause of the clubbing. Mild clubbing without cyanosis is a frequent finding in subacute bacterial endocarditis, where it may appear a few weeks after the disease develops, disappearing with therapy. Clubbing also occurs in noncardiac conditions, such as bronchiectasis, abscess or carcinoma of the lungs, and other chronic pulmonary lesions, cirrhosis of the liver, chronic ulcerative colitis, etc Clubbing may also occur as a familial trait in otherwise normal people. Clubbing does not occur in cases of acquired valvular disease with failure, even if cyanosis is present.

The exact cause of clubbing is unknown, though it has recently been shown that the capillaries of the soft parts are dilated in all types of clubbing except familial, and that there is an abnormally high blood flow through the finger tips Unilateral clubbing has been reported in aneurism of the arch of the aorta or of the subclavian artery, but arteriovenous fistulas usually

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do not cause clubbing. Clubbing of the toes may also occur, but it should be sought in the big toe because the other toes may seem clubbed normally

Subcutaneous Nodules (Fig. 36).—Subcutaneous nodules vary from pinhead to bean size. They lie beneath the skin and over tendon sheaths, especially over bony prominences, and near the extensor aspects of large joints such as the elbow, wrist, knee and ankle. They are also found along the spine and even on the scalp. The nodules on the extremities tend to be symmetrical in distribution Since they are subcutaneous, they can be made to glide under the skin. If the skin over them is made taut, they appear as pale, hard prominences.

Subcutaneous nodules occur in active rheumatic fever and in rheumatoid arthritis. They are analogous to the Aschoff bodies which occur in the myocardium The nodules may last from a few days to several months.

Recent experimental studies have indicated that subcutaneous nodules may develop as a manifestation of the unihibited action of proteolytic enzymes such as trypsin on the mesenchymal tissue The enzymes may be released as part of the general allergic response of the body to the rheumatic process.

Osler Nodes.—Osler nodes usually occur in the pads of the fingers and toes. They are red, papular, painful, erythematous nodules, 0 5 to 1 5 cm. in diameter, often pale in the center They are usually intracutaneous but may be subcutaneous. They may occur in crops, and disappear in a few hours or a day Rarely they suppurate, leaving a small ulcer. More often they gradually change from a red to a bluish color and may leave a slight brown stain Occasionally a small scab forms, which may be picked off

They occur in acute or subacute bacterial endocarditis and are due either to minute emboli in the superficial terminal vessels of the skin or to an arteritis of the smaller vessels.

Tender Fingers and Toes.—When the emboli are deep, there occur localized pain and tenderness in one or more of the fingers and toes, but no swelling or redness occurs.

Janeway Lesions.—These occur in acute and subacute bacterial endocarditis. They are small erythematous and partially hemorrhagic, macular and papular lesions, 1 to 4 mm in diameter. They appear on the palms, soles or finger tips or plantar surfaces. They are not tender or painful

Petechiæ.—Petechiæ or so-called petechial hemorrhages frequently appear on the hands and forearms, in the webs of the toes, but can be found anywhere on the skin, and mucous membranes, such as the conjunctiva, mouth, *etc.* Under the nails they are linear in shape, 4 to 5 mm long, and are known as splinter hemorrhages.

Petechiæ can be produced in two ways: there may be weakness and aneurismal dilatations of the capillary wall. This is the reason petechiæ disappear without producing tell-tale black and blue marks of hemorrhage. Such petechiæ are not specific for subacute bacterial endocarditis and occur in normal people, rheumatic fever, and many other noncardiac conditions, associated with increased capillary fragility. Petechiæ with a white center are usually due to small emboli However, they may occur in the absence of emboli as in hemorrhagic diseases.

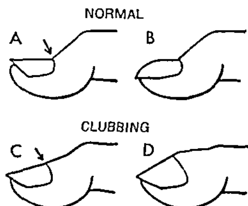


FIG 35 —The differentiation between normal and clubbed fingers (after Lovibond). A, and B, are normal In A, the angle at the base of the nail is about 160°. In B, the nail is curved but there is no clubbing because the angle at the base of the nail is preserved

C, and D, show clubbing. In C, the clubbing is moderate; in D, marked clubbing is present



FIG 36 —Subcutaneous nodules in the scalp of a young child (Kindness of Dr. K. Merritt)

artery becoming palpable (page 54). This has no significance Occasionally two pulsations with each heart beat are due to the percussion and tidal waves (page 53) of the radial pulse (*pulsus bisferiens*). This occurs with lesions of the aortic valve, but can only be determined from the radial arteriogram. In such cases, other more reliable signs of aortic valvular disease are also present.

Irregularity of the Pulse.—Many of the cardiac arrhythmias can be diagnosed merely by taking the pulse and simultaneously noting the jugular vein pulsations. This is discussed further on page 150. However, palpation of the pulse alone is often valuable. For example, a ventricular premature contraction is usually felt as two beats in quick succession (the normal beat and the premature beat) followed by a long pause. With most auricular premature contractions, there are two beats in quick succession followed by a fairly short pause. In auricular fibrillation, the pulse is usually totally irregular in rate, rhythm and the force of the radial pulsation, and if one palpates the radial artery patiently, long pauses will occur which were not preceded by two beats in quick succession. A *pulse deficit*, namely a greater pulse rate at the apex of the heart than at the radial artery has value in diagnosing auricular fibrillation if the difference is 10 or more beats per minute However, a pulse deficit can occur with ventricular premature contractions, if they are too weak to cause the semilunar valves to open (frustrane beats).

Pulsus Paradoxicus.—Pulsus paradoxicus, or paradoxical pulse refers to the phenomenon in which the peripheral pulse is markedly diminished or even abolished during ordinary or quiet inspiration. The pulse promptly appears during expiration It can be best detected by the use of a sphygmomanometer, the cuff being inflated to a point 5 to 10 mm less than the systolic blood pressure. Careful auscultation over the brachial artery will disclose the decrease or abolition of the pulse during inspiration Small variations should be ignored

Pulsus paradoxicus is characteristically found in acute pericardial effusion, or in chronic constrictive pericarditis It can also occur without cardiac pathology as in cases of laryngeal stenosis, or severe asthma, *etc.* A similar though less marked diminution in the pulse occurs normally during forced inspiration For this reason the term "paradoxical" is a poor one.

Pulsus paradoxicus, regardless of its etiology, occurs when there is a marked discrepancy between the pulmonary blood volume during expiration, and the pulmonary vascular capacity during inspiration. Thus with pericardial effusion or constrictive pericarditis, the right ventricle has a decreased output and the systemic circulation becomes distended with blood, but the pulmonary bed remains relatively unfilled With inspiration, the blood-holding capacity of the lungs increases so much that enough blood is drawn into the lungs to make the systemic pressure fall temporarily. (Even in a normal person, inspiration increases the blood-holding capacity of the lung.) The pulsus paradoxicus of laryngeal stenosis or severe asthma can be similarly explained. Here, the extreme dyspnea causes a very high negative intrathoracic pressure which draws an abnormally large quantity of blood into the lungs during inspiration.

ABNORMAL PULSE FINDINGS

The Collapsing (Corrigan) Pulse.—This is also known as the water-hammer pulse. It is best appreciated when the arm is raised above the head. The pulse wave strikes the finger with a sudden, sharp jerk and then abruptly collapses. A thrill may also be palpable. The collapsing pulse is characteristic of aortic insufficiency but may occur in any condition with a large pulse pressure and a low diastolic pressure, such as patent ductus arteriosus, hyperthyroidism, fever, *etc*.

Capillary Pulsation.—Capillary pulsation frequently but not necessarily accompanies a collapsing pulse. It can be detected by making gentle pressure on the nails, which brings out a rhythmic flush of the nail bed. The lips and skin may also show capillary pulsation. This can be elicited by placing a glass slide gently on the lips or rubbing the skin of the forehead or abdomen. The resultant hyperemic area blushes and pales alternately, each blush being synchronous with the pulse.

Capillary pulsation is due to local or general vasodilatation and its occurrence in aortic insufficiency is due to the fact that marked vasodilatation is also present, because it can be produced in normal people by warming the hand or skin in water. Marked capillary pulsation may also occur in hyperthyroidism and in an arteriovenous fistula.

Thrills.—A thrill over the brachial, radial, femoral or any peripheral artery may occur in aortic insufficiency, arteriovenous fistula, aneurism, or in any condition where the pulse pressure is very large and the rate rapid.

The Plateau Pulse.—This rises slowly but firmly to meet the finger. It has been described as characteristic of aortic stenosis. However, it is more often absent than present in aortic stenosis. The radial arteriogram of the plateau pulse is very characteristic and shows a slow initial upstroke with a sharp notch, the anacrotic notch.

Inequality of the Pulse.—Bilateral inequality of the pulse is usually normal, but may occur with aneurism of the aortic arch, atypical coarctation of the aorta, a cervical rib, or the scalenus anticus syndrome.

The Scalenus Anticus Syndrome.—This is produced by compression of the subclavian artery between the bellies of the anterior and middle scalene muscles, or between the muscle and the first rib. The radial artery pulse can be frequently obliterated by having the patient turn his face toward the side being examined, then take a deep breath and hold it while the neck is extended (Adson maneuver). In addition to the pulse abnormality, pain, paresthesias over the distribution of the brachial plexus, muscular atrophy, especially of the small muscles of the hand, and occasionally gangrene of one or more of the fingers may occur with the syndrome. When the scalenus anticus syndrome is present on the left side, the occurrence of precordial pain and the left arm signs may simulate angina pectoris.

When bilateral inequality of the pulse is sought, it is preferable to palpate the brachial rather than the radial arteries because variations in the depth of the radial artery may produce bilateral inequality of the pulse normally.

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Abnormal Femoral Pulses.—A small femoral pulse occurs in coarctation of the aorta. In addition the femoral pulse wave is felt after the radial pulse A similar condition prevails in embolism or thrombosis of the abdominal aorta, or of the iliac or femoral artery. Marked pulsation of the femoral artery occurs with aortic insufficiency and in any case with a large pulse pressure.

ABNORMAL BLOOD PRESSURE FINDINGS

High blood pressure is usually considered present when the systolic pressure is over 150, or the diastolic pressure over 100. The many causes of high blood pressure are described on page 556. Here I merely wish to discuss some of the factors which can cause transient variations in blood pressure, high or low

Normal variations in blood pressure have already been discussed on page 27. Fluctuations from beat to beat occur in auricular fibrillation, and in any condition where the rhythm is irregular Paroxysmal hypertension may occur with pheochromocytoma (page 701). However, during an attack of acute pulmonary edema, the systolic pressure may rise 90 mm. or more, with a marked increase in diastolic pressure also. One of my patients, an elderly woman, had a resting pressure of 140/90, which regularly rose to 250/120 during attacks of pulmonary edema In chronic heart failure, the pressure may either rise, fall or remain more or less stationary. In hypertensives who develop heart failure, the pressure frequently falls, to rise again when compensation is restored

A marked drop in pressure occurs characteristically with acute myocardial infarction, but it may be delayed for several hours or a day after the infarct A rise in pressure immediately after myocardial infarction has also been reported, but I have not observed this. However, a rise, even marked, does occur with attacks of angina pectoris. Thus, when a patient with angina pectoris develops a fall in pressure during an anginal seizure, it is a presumptive sign of myocardial infarction A drop in blood pressure also occurs in acute pericardial effusion, due to the decreased cardiac output, and a drop in pressure may occur with syncope and shock from any cause.

A normal or elevated blood pressure in the upper extremities with a low femoral blood pressure is a sign of coarctation of the aorta, or embolism, thrombosis, or aneurism of the abdominal aorta, or of the iliac or femoral artery On the other hand, in normal people, and especially aortic insufficiency, the femoral systolic pressure may be very much higher than the brachial. Marked bilateral variations in blood pressure have the same cause as variations in the radial pulse (page 140).

The most common cause of an increased pulse pressure—more than 80 mm —is essential hypertension, where the pressure, for example, may be 280/160. When the systolic pressure is near normal, aortic insufficiency, patent ductus arteriosus and marked vasomotor dilatation give a large pulse pressure. A small pulse pressure—less than 25 mm.—occurs when the systolic pressure is low as in pericarditis with effusion, Addison's disease, shock, infants and young children, rarely aortic stenosis Occasionally a small pulse pressure occurs in hypertension when there is a marked rise in diastolic pressure.

Pulsus paradoxicus may also occur normally in a mechanical way. In such cases, deep inspiration elevates the thorax and causes the subclavian artery to be compressed between the first rib and the clavicle, thereby reducing or abolishing the radial pulse

Pulsus Alternans.—Pulsus alternans, or alternans of the heart is a sequence of strong and weak pulse beats at the radial artery. There is characteristically a longer interval between the strong pulse and the succeeding weak pulse, than between the weak pulse and the succeeding strong pulse. This is an important sign, because if premature contractions occur alternately, a sequence of strong and weak (premature) beats may occur, but here, the interval between the strong and the weak is shorter than between the weak and the strong beats. The irregularity of the rhythm in pulsus alternans is due to the slower spread of the smaller pulse wave to the radial artery. This can be easily demonstrated because at the apex the rhythm is completely regular. Occasionally the rhythm at the radial artery is also regular.

Pulsus alternans can often be detected when the blood pressure is measured. If the cuff is inflated above the systolic pressure and deflated slowly until the sounds are first heard, these sounds correspond to the stronger pulses and the rate will be one half that obtained when the cuff is deflated to the point where the weak beats can come through. The difference between the systolic pressure of the strong and weak beats is usually 5 or 10 mm , but may be as much as 30 or 40 mm

Pulsus alternans can be recorded by means of a radial arteriogram. In the electrocardiogram, there is usually no difference between the weak and strong beats (Occasionally electrical alternans is also present. In such a case, the shape of the *QRS* and even the *T* vary in alternate beats. However, electrical alternans may occur without pulsus alternans) On auscultation, there may or may not be alternation of the intensity of the heart sounds, or of murmurs, if present.

Alternans appears in heart failure, coronary artery disease, hypertension, and paroxysmal tachycardia, but is rare in acute myocardial infarction The exact cause of alternans is obscure. It may be due to an alternate rather than a regular contraction of some of the cardiac fibers. In the past, its presence has been considered a grave sign. This is by no means so Furthermore alternans during an attack of paroxysmal tachycardia is of no consequence Similarly if alternans is due to transient intermittent bundle branch block, it has no clinical significance I also believe that pulsus alternans which occurs for a few beats after a premature contraction is likewise insignificant

Pulsus Bigeminus.—In pulsus bigeminus (bigeminal pulse), a succession of two beats is followed by a pause Although this is usually due to ventricular premature contractions occurring every other beat, it can be produced by auricular premature contractions occurring every other beat, and by various forms of *a–v* block, in which every third beat drops out Similarly, a sequence of three beats followed by a pause (pulsus trigeminus), or a sequence of four beats followed by a pause (pulsus quadrigeminus) is also not pathognomonic of ventricular premature contractions.

The differentiation of pulsus bigeminus due to ventricular premature contractions and pulsus alternans is described above.

Abnormal Femoral Pulses.—A small femoral pulse occurs in coarctation of the aorta. In addition the femoral pulse wave is felt after the radial pulse. A similar condition prevails in embolism or thrombosis of the abdominal aorta, or of the iliac or femoral artery. Marked pulsation of the femoral artery occurs with aortic insufficiency and in any case with a large pulse pressure.

ABNORMAL BLOOD PRESSURE FINDINGS

High blood pressure is usually considered present when the systolic pressure is over 150, or the diastolic pressure over 100. The many causes of high blood pressure are described on page 556. Here I merely wish to discuss some of the factors which can cause transient variations in blood pressure, high or low

Normal variations in blood pressure have already been discussed on page 27. Fluctuations from beat to beat occur in auricular fibrillation, and in any condition where the rhythm is irregular Paroxysmal hypertension may occur with pheochromocytoma (page 701). However, during an attack of acute pulmonary edema, the systolic pressure may rise 90 mm. or more, with a marked increase in diastolic pressure also One of my patients, an elderly woman, had a resting pressure of 140/90, which regularly rose to 250/120 during attacks of pulmonary edema. In chronic heart failure, the pressure may either rise, fall or remain more or less stationary. In hypertensives who develop heart failure, the pressure frequently falls, to rise again when compensation is restored.

A marked drop in pressure occurs characteristically with acute myocardial infarction, but it may be delayed for several hours or a day after the infarct A rise in pressure immediately after myocardial infarction has also been reported, but I have not observed this However, a rise, even marked, does occur with attacks of angina pectoris. Thus, when a patient with angina pectoris develops a fall in pressure during an anginal seizure, it is a presumptive sign of myocardial infarction A drop in blood pressure also occurs in acute pericardial effusion, due to the decreased cardiac output, and a drop in pressure may occur with syncope and shock from any cause

A normal or elevated blood pressure in the upper extremities with a low femoral blood pressure is a sign of coarctation of the aorta, or embolism, thrombosis, or aneurism of the abdominal aorta, or of the iliac or femoral artery. On the other hand, in normal people, and especially aortic insufficiency, the femoral systolic pressure may be very much higher than the brachial Marked bilateral variations in blood pressure have the same cause as variations in the radial pulse (page 140)

The most common cause of an increased pulse pressure—more than 80 mm—is essential hypertension, where the pressure, for example, may be 280/160 When the systolic pressure is near normal, aortic insufficiency, patent ductus arteriosus and marked vasomotor dilatation give a large pulse pressure. A small pulse pressure—less than 25 mm—occurs when the systolic pressure is low as in pericarditis with effusion, Addison's disease, shock, infants and young children, rarely aortic stenosis. Occasionally a small pulse pressure occurs in hypertension when there is a marked rise in diastolic pressure.

Pulsus paradoxicus may also occur normally in a mechanical way. In such cases, deep inspiration elevates the thorax and causes the subclavian artery to be compressed between the first rib and the clavicle, thereby reducing or abolishing the radial pulse.

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The differentiation of pulsus bigeminus due to ventricular premature contractions and pulsus alternans is described above.

The systolic component is due to the aortic insufficiency. The diastolic component is due to sudden distention of the femoral vein during diastole, as a result of the tricuspid insufficiency.

Continuous Arterial Bruits.—A *continuous bruit, associated with a systolic or a continuous thrill, heard over a peripheral artery is characteristic of an arteriovenous fistula.* In an aneurism of a peripheral artery, a systolic and a diastolic murmur may appear, but there is a pause between the systolic and diastolic *components* The *normal venous hum* (page 35) should not be confused with a continuous arterial bruit

ABNORMAL PHYSICAL FINDINGS IN THE HEAD AND NECK

Abnormal Facies.—Myxedema is associated with a very characteristic facies, namely an apathetic appearance, coarse, dry, puffy skin, and puffiness *of the eyelids* The *subcutaneous tissue generally* has a *puffy, non-pitting* consistency The hair is dry, scanty, and the eyebrows tend to lose their hair.

Abnormalities of the Eyes.—Irregularity of the *pupils, or failure* of the pupils to react to light but a response to accommodation (Argyll-Robertson pupil) due to central nervous system syphilis, may lead one to the diagnosis of syphilitic heart disease Similarly, bilateral exophthalmus and the *other signs of hyperthyroidism, namely infrequent winking (Stellwag's* sign), weakness on convergence (Mobius' sign), delay or failure of the upper lid to follow the eyeball on looking downward (von Graefe's sign) retraction of the upper lid (Dalrymple's sign), puffiness of the lids, *etc* , may explain the appearance of paroxysmal auricular fibrillation or of refractory heart failure However, bilateral exophthalmos can be simulated in patients with chronic nephritis who do not have any thyroid disturbance In such *patients, the most outstanding sign is the marked retraction of the* upper lid.

The presence of petechiæ in the conjunctiva as a sign of bacterial endocarditis has already been mentioned (page 139). The petechiæ should be sought by everting the lids.

Ophthalmoscopic Examination (see also page 559).—Ophthalmoscopic examination should be routinely performed, certainly in every hypertensive *patient, or patient complaining of headache or visual disturbance* Below are described the normal and some of the more common findings in cardiovascular disease and associated conditions·

Normal Ophthalmoscopic Findings.—The most obvious *landmark* of the fundus is the optic nerve head or disc, which ordinarily shows a sharp outline, but may show a slightly indistinct border on the nasal side The center of the disc may be somewhat pale, or whitish, and may be somewhat depressed below the level of the border of the disc. This is known as the "physiological cup."

The branches of the central artery and vein radiate from the disc Arteries and veins can be distinguished by their color. *The arteries are slightly* smaller than the veins, the arterio-venous or a-v ratio being 4.5, or 2.3 The arteries show along their middle a fine streak of light reflected from the anterior surface of the arterial media and the anterior surface of the

Although the normal bilateral difference in blood pressure is 10 mm., differences as great as 40 mm. systolic, and 20 mm. diastolic, have been reported in patients with hypertension. However, when such marked bilateral variations in blood pressure are present, one should search for an aneurism of the arch of the aorta or adjacent vessel, atypical coarctation of the aorta, a cervical rib or the scalenus anticus syndrome.

ABNORMAL VASCULAR SOUNDS

Abnormal Neck Vessel Sounds.—The normal vascular sounds in the neck were described on page 35. Abnormal sounds in the neck vessels can occur in the following ways:

1. Transmission of murmurs from the base of the heart. Loud systolic aortic and pulmonary murmurs are transmitted well to the neck. I recently saw a case of congenital stenosis of the infundibulum of the right ventricle proven with angiocardiographic studies, in which the systolic murmur was almost as loud in the neck as over the second and third left intercostal spaces. However, while aortic diastolic murmurs are transmitted well to the neck, pulmonary diastolic murmurs are transmitted poorly.

2 Abnormalities of the blood vessels of the neck and thorax, such as aneurism of the subclavian artery, or of the aorta, coarctation of the aorta, patent ductus arteriosus, *etc*, can cause loud systolic murmurs in the neck. However, a more common cause of a marked pulsation and systolic murmur in the right side of the neck is kinking of the common carotid artery, which occurs in association with hypertensive heart disease (page 148)

Duroziez's Sign.—Duroziez's sign consists of a diastolic murmur heard over peripheral arteries, such as the femoral or brachial artery, when slight pressure is made with the stethoscope bell. This is heard in conjunction with a normal systolic vascular bruit

Duroziez's sign occurs in two types of conditions:

1. **Aortic Insufficiency.**—There is an increased diastolic flow of blood back to the heart. Therefore if a blood pressure cuff is put on distally to the point where the vessel is being auscultated, and inflated to a subdiastolic level, the murmur increases. This is due to the fact that the blood, being sucked back to the heart must pass through compressed vessels. If the diastolic pressure is 0, the cuff should be inflated to 20 or 30 mm.

2 **Peripheral Vasodilatation.**—In peripheral vasodilatation due to fever, anemia, thyrotoxicosis, or in vasodilatation produced in normal people by immersing the limbs in hot water, there is an increased diastolic flow of blood forward. Thus, when a blood pressure cuff, at a subdiastolic pressure, is placed distal to the vessel being auscultated, it decreases and obliterates the diastolic murmur, because less blood is able to go forward during diastole.

In cases of either aortic insufficiency or peripheral vasodilatation, the sudden distention of the arteries during systole produces a cracking noise, known as a pistol-shot sound. It has no value in diagnosis because it occurs in any case where the pulse pressure is large and the diastolic pressure is low. In combined aortic insufficiency and tricuspid insufficiency, a systolic and diastolic pistol shot sourd may be heard in the groin (Traube's sound)

The systolic component is due to the aortic insufficiency. The diastolic component is due to sudden distention of the femoral vein during diastole, as a result of the tricuspid insufficiency.

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column of blood in the vessels The veins have a much less distinct light reflex The caliber of the vessels decreases gradually toward the macula and toward the periphery of the fundus.

The macula is located on the temporal side of the disc, at a distance of about two disc diameters from the disc. It is often somewhat darker in color than the rest of the fundus, and there are no visible blood vessels in its central portion At the center, a brilliant point of light reflex, marking the fovea centralis may appear. This should not be mistaken for an exudate.

Retinal Arteriosclerosis.—Sclerosis of the retinal arteries can cause the following changes:

1 Changes in the light reflex. Increased brightness of the arteries may appear, giving the vessels the appearance of burnished copper wire. In more advanced cases, the entire vessel shines bright and white, like a silver wire, and no sign of the red blood column within the vessel is evident. In other cases, the light reflex becomes irregular, showing dots and beading.

2 Sheathing of the arteries This consists of white lines which run along the vessel wall In advanced stages, the whole vessel resembles a white, fibrous cord Sheathing may occur normally in arteries near the disc. When it occurs away from the disc, it is pathological. It is especially noted where the arteries cross the veins.

3 Irregularity of the arterial lumen This may occur, as well as tortuosity and general thinness of the arteries

4 Interruption of the veins The veins appear interrupted where the arteries pass over them, and may be dilated peripheral to these points of arterio-venous crossing.

5 The disc remains normal.

Arteriosclerotic Retinopathy.—When the blood supply to the retina becomes inadequate, the arteriosclerotic vessels undergo further changes, and hemorrhages and exudates appear The hemorrhages are small, flame-shaped, or feathery, and are scattered throughout the fundus. The exudates, which actually are degenerative and proliferative rather than exudative, are small, bright, white or yellow spots, seen especially in the center of the fundus The optic nerve remains normal

Hypertensive Retinopathy.—This occurs in malignant hypertension, chronic glomerulonephritis and also in toxemias of pregnancy It is characterized by marked edema of the disc and of the retina, marked exudation and hemorrhages. The margins of the edematous disc are blurred due to the edema. Retinal edema is noted by the pale or grayish cloudiness of the affected portion of the fundus. The exudates, known as cotton-wool exudates, are soft masses, irregular in shape, gray-white, and with fluffy margins, and are scattered throughout the fundus. These exudates later may become completely absorbed or are transformed into yellow, more sharply outlined spots

Because the edema also collects between the radially arranged fibers about the macula, sharp white spots appear radiating, star-like around the macula Non-characteristic flame-shaped hemorrhages also appear throughout the fundus.

Hypertensive retinopathy may be and often is associated with arteriosclerosis and arteriosclerotic retinopathy, but may occur without marked

vascular changes, especially in nephritis. There is often also present a very characteristic reduction in caliber of the entire retinal arterial tree due to spasm.

Diabetic Retinopathy.—Diabetes may produce specific changes in the retina. These changes consist of deep round hemorrhages which differ from the flame-shaped hemorrhages of arteriosclerosis and hypertension, and which actually are not hemorrhages but aneurismal dilatations of the vessel walls. In addition characteristic, solid, soapy or waxy, glistening round or oval exudates appear in a rough circle around the macula. The disc remains normal, as do the vessels.

Papilledema, or Choked Disc.—This consists of the swelling of the disc due to increased intracranial pressure, usually from brain tumors. It differs from hypertensive retinopathy in that the disc is elevated above the rest of the fundus, its margin is blurred, and the vessels show a distinct bend as they cross the disc margin. The surrounding retina may be edematous, the veins are engorged and tortuous, and hemorrhages may occur, especially around the disc, but the arteries are normal.

Cyanosis Retinæ.—Marked changes may occur in the fundus in cases of cyanotic congenital heart disease. The entire fundus has a rosy, bluish tinge, the small vessels and capillaries are dilated, elongated and tortuous. Since more of them than usual are filled with blood, the vessels appear more numerous, that is, closer together The arterioles as well as the veins become dilated and tortuous, and may have the same bluish color as the veins, helping to confirm the diagnosis of a venous-arterial shunt In some cases, the arterioles remain narrow and relatively pale, in contrast to the dilated venules which may show a bright light reflex. The disc may be markedly edematous

Abnormal Physical Findings in the Nose and Mouth.—Patients with chronic rheumatic heart disease occasionally show perforation of the nasal septum This is actually traumatic in origin and is due to repeated bouts of epistaxis, the patient picking off the scab which forms on the septum.

The mouth does not usually show important cardiovascular signs except petechiæ which may appear on the soft and hard palates, and dilatation of the veins on the under surface of the tongue which may appear with right ventricular failure or with marked elevation of the venous pressure above 200 mm. of water.

Abnormal Physical Findings in the Neck.—It is sometimes important to determine diffuse or localized enlargement of the thyroid gland The isthmus and both lobes should be palpated. To facilitate palpation, one hand should displace the trachea to the side being palpated, to help the palpating hand outline the lobes of the thyroid gland. When diffuse enlargement of the thyroid is present as in Graves' disease, a systolic bruit can be heard over the gland, which may pulsate strongly.

The Tracheal Tug.—The trachea may be displaced from the midline by an aneurism of the arch of the aorta In addition if an aneurism of the arch of the aorta becomes adherent to the trachea, a tracheal tug (Oliver's sign) ✓ may occur. The patient, lying in bed, lifts his chin, and the examiner grasps the larynx firmly in his fingers. When an aneurism is present, there may be a downward tugging of the larynx with each heart beat, due to the pulsation of the aneurism over the bifurcation of the trachea

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Abnormal Physical Findings in the Nose and Mouth—Patients with chronic rheumatic heart disease occasionally show perforation of the nasal septum. This is actually traumatic in origin and is due to repeated bouts of epistaxis, the patient picking off the scab which forms on the septum.

The mouth does not usually show important cardiovascular signs except petechiæ which may appear on the soft and hard palates, and dilatation of the veins on the under surface of the tongue which may appear with right ventricular failure or with marked elevation of the venous pressure above 200 mm. of water.

Abnormal Physical Findings in the Neck.—It is sometimes important to determine diffuse or localized enlargement of the thyroid gland The isthmus and both lobes should be palpated. To facilitate palpation, one hand should displace the trachea to the side being palpated, to help the palpating hand outline the lobes of the thyroid gland When diffuse enlargement of the thyroid is present as in Graves' disease, a systolic bruit can be heard over the gland, which may pulsate strongly.

The Tracheal Tug.—The trachea may be displaced from the midline by an aneurism of the arch of the aorta In addition if an aneurism of the arch of the aorta becomes adherent to the trachea, a tracheal tug (Oliver's sign) ✓ may occur. The patient, lying in bed, lifts his chin, and the examiner grasps the larynx firmly in his fingers. When an aneurism is present, there may be a downward tugging of the larynx with each heart beat, due to the pulsation of the aneurism over the bifurcation of the trachea.

A tracheal tug is not pathognomonic of an aneurism of the aortic arch and can occur with any condition (neoplasm, infection, *etc.*) which anchors the trachea or left bronchus to the aorta

Kinked Carotid Artery.—In hypertensive patients, especially women, a marked pulsation frequently occurs at the base of the neck on the right side. There may also be a loud bruit and thrill present. These findings are due to kinking of the right common carotid artery It is due to elevation of the arch of the aorta, and is not due to an aneurism. Strong pulsation of the carotid artery also occurs in aortic insufficiency, patent ductus arteriosus, hyperthyroidism, anemia, fever, and tachycardia from any cause.

Neck Vein Engorgement.—Engorgement of the neck veins in the upright position is abnormal (see page 108). It occurs when the venous pressure is elevated and thus appears in right-sided heart failure, acute pericardial effusion with pericardial tamponade, chronic constrictive pericarditis, and with any condition producing obstruction of the superior vena cava (see page 672). Occasionally with right-sided heart failure (with or without tricuspid insufficiency), systolic pulsation of the distended neck veins occurs, (see below). In cases of obstruction of the superior vena cava, pericardial effusion or chronic constrictive pericarditis, pulsations of the distended neck veins are minimal

Inspiratory Filling of the Neck Veins.—Inspiratory filling of the neck veins can occur in the following conditions:

1 *Severe Right-Sided and Left-Sided Heart Failure.*—Normally on inspiration the negative intrathoracic pressure exerts a sucking effect on the peripheral venous system, thus increasing the venous return to the heart. A normal right ventricle, in accord with Starling's Law (page 195), dilates to accommodate the increased volume of blood and propels it into the lungs without causing any increase in venous pressure In cases of severe left-sided and right-sided heart failure, the weakened right ventricle is already dilated and is unable to expel all the blood it receives during inspiration into the lungs, which are already congested because of the associated left-sided heart failure. Inspiratory filling of the neck veins therefore occurs

2 *Superior Vena Cava Obstruction.*—When obstruction of the superior vena cava occurs at or below the point of entrance of the azygos vein into it (see page 672), the venous drainage from the upper part of the body to the right heart is by way of the superficial veins of the thorax and abdomen into the inferior vena cava. On deep inspiration, the descent of the diaphragm tends to compress the inferior vena cava, interfering with the flow of blood into it from the veins of the upper half of the body so that the pressure in the neck veins rises

This inspiratory filling of the neck veins can be enhanced by placing a Levine tube tightly around the thorax at the level either of the nipples or the xiphoid process This also interferes with the flow of blood downward through the collateral superficial veins of the thorax.

When obstruction of the superior vena cava occurs above the point of entrance of the azygos vein into it, blood from the upper half of the body reaches the right auricle principally by way of the azygos vein and the proximal patent portion of the superior vena cava, so that inspiratory filling of the neck veins does not occur.

3. *Chronic Constrictive Pericarditis, and Pericardial Effusion With Pericardial Tamponade.*—Here inspiration increases the venous return to the heart, but the right ventricle is unable to dilate adequately to receive the blood because of the thickened pericardial sac, or the pericardial effusion.

When inspiratory filling of the neck veins occurs in chronic constrictive pericarditis or in pericardial effusion, pulsus paradoxicus (page 141) may also be present. This does not occur in the other conditions associated with inspiratory filling of the neck veins.

Abnormal Neck Vein Pulsations.—The normal venous pulsation with its systolic collapse was described on page 34. This type of pulsation is sometimes called the auricular form of the venous pulse, in contrast to the ventricular form of the venous pulse, which occurs in cases of right-sided heart failure, tricuspid insufficiency, nodal rhythm, paroxysmal auricular or nodal tachycardia and in auricular fibrillation.

The Ventricular Form of the Venous Pulse.—Here, only one wave occurs, a sustained systolic plateau, which collapses momentarily in diastole. This can occur in the following conditions:

1. *Right-Sided Heart Failure.*—In cases of right ventricular failure and an elevated venous pressure, the auricles remain distended and do not fully empty in diastole. With auricular systole, the jugular *a* wave is not marked because the auricles are too distended to contract effectively. When ventricular systole occurs and the *a–v* valves are pulled down, the auricular pressure also does not decrease and the systolic collapse does not occur. The pressure in the auricles and jugular vein does fall momentarily at the beginning of diastole when the *a–v* valves open. However, the diastolic collapse is of very short duration and the systolic plateau is much more prominent.

2. *Auricular Fibrillation.*—Here the auricles do not contract effectively and remain in a functional state of diastole. Therefore, no jugular *a* wave appears, and effective auricular emptying occurs only during the early phase of diastole, so that a systolic plateau appears, interrupted by a sharp but transient diastolic collapse of the neck veins.

3. *Tricuspid Insufficiency.*—In tricuspid insufficiency, the blood regurgitating from the right ventricle into the right auricle and superior vena cava actually produces a marked systolic pulsation in the jugular vein, and may even cause the lobes of the ear to pulsate with each heart beat. This systolic pulsation in the jugular vein can be demonstrated by compressing the vein with a finger and expressing blood from the vein from below upwards. The segment above the finger remains distended, and the segment below the finger shows rhythmic systolic filling.

This systolic venous pulsation can sometimes be noted as far away as the dorsal veins of the hands. To elicit pulsations in the dorsal veins of the hands, the hand should be raised gently just above the level where the veins collapse. Pulsation of the dorsal veins of the hand, however, is not pathognomonic of tricuspid insufficiency and may occur in any case of severe right-sided heart failure.

4. *Nodal Rhythm.*—See below.

5. *Paroxysmal Auricular or Nodal Tachycardia.*—See page 343.

A tracheal tug is not pathognomonic of an aneurism of the aortic arch and can occur with any condition (neoplasm, infection, *etc.*) which anchors the trachea or left bronchus to the aorta.

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3 *Incomplete A-V Block* (2:1, 3:1, *type, etc.*) (*Fig.* 37).—With each pulse beat, the jugular veins show a systolic collapse, but since the auricles are beating faster than the ventricles, additional *a* waves can be seen during diastole, in the intervals between radial pulse beats By counting the *a* waves and the radial pulse, the exact degree of *a–v* block can frequently be determined. Occasionally the Wenckebach type of *a–v* block (page 325) can be similarly diagnosed.

4. *Complete A-V Block* (*Fig.* 37).—With each radial pulse beat, the jugular veins show a systolic collapse, and additional *a* waves occur in the interval between pulse beats, just as with incomplete *a–v* block. However, since complete *a–v* block is present, some of the auricular contractions occur during ventricular systole and when the *a–v* valves are closed, causing a large systolic jugular pulsation. Since the auricular rate is faster than the ventricular, indicating *a–v* block, the large pulsation indicates that the block is complete, because in incomplete *a–v* block, every auricular beat that is followed by a ventricular beat occurs at a fixed interval before the ventricular beat, and the auricles and ventricles cannot contract simultaneously

5. *Auricular Fibrillation* —Auricular fibrillation with a slow, almost regular ventricular rate may occur after full digitalization. In such cases, the ventricular form of jugular pulse is present, which alone is suggestive of auricular fibrillation Furthermore the ventricular rhythm is not as regular as in the above four conditions

B. Neck Vein Pulsations in Other Arrhythmias —In auricular flutter, rapid, regular, shallow jugular waves appear, due to the flutter, but the pulse rate is much slower because some degree of *a–v* block is usually pre-present

In auricular or ventricular premature contractions, the pulse may be very irregular and may resemble auricular fibrillation However, if the irregularity of the pulse is due to either auricular or ventricular premature contractions, the neck veins show a normal systolic collapse with the regular beats, indicating that the auricles are contracting, and that the basic rhythm is of sinus origin As a matter of fact, whenever the ventricular rate is irregular and the jugular veins show a systolic collapse, auricular fibrillation can be ruled out. The use of the radial pulse alone to differentiate auricular fibrillation from premature contractions is described on page 141.

ABNORMAL PHYSICAL SIGNS IN THE HEART AND LUNGS,

Hyperpnea.—Hyperpnea consists of an exaggerated depth of respiration without any symptoms of respiratory distress. It may occur in pulmonary or cardiac conditions associated with a decreased vital capacity or with pulmonary congestion, but may also be present in noncardiac conditions, such as diabetic or uremic acidosis, severe anemia, shock, *etc.* In such cases regardless of the degree of hyperpnea, there is no orthopnea because there is no pulmonary congestion

Cheyne-Stokes Respiration.—Cheyne-Stokes respiration, or periodic breathing, consists of a sequence of periodic apnea and hyperpnea. The

The Use of Neck Vein Pulsations in the Diagnosis of Cardiac Arrhythmias.—By simultaneously palpating the radial artery and noting the character of the neck vein pulsations, it is possible to diagnose many of the common arrhythmias. The reason for this is that the radial pulse indicates the ventricular rhythm, and the neck vein pulsations indicate the auricular rhythm.

The value of the radial artery and neck vein pulsations in the diagnosis of arrhythmias can be illustrated by the following examples:

A When the radial pulse is very slow and regular, five possible rhythms may be present: sinus bradycardia, nodal rhythm, incomplete *a–v* block of

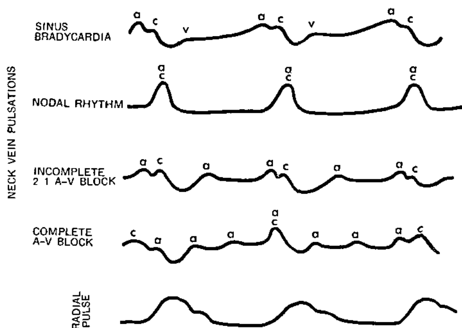


FIG 37 —Neck vein pulsations in some common arrhythmias with a slow ventricular rate. The radial pulse is also shown. See text for details.

the 2·1, 3:1, *etc.*, type, complete *a–v* block, or auricular fibrillation with a slow ventricular rate.

1 *Sinus Bradycardia* (*Fig.* 37) —A characteristic systolic collapse of the neck veins appears with each radial pulse, indicating that the auricles are contracting effectively and normally. (However, if right-sided heart failure or tricuspid insufficiency is present, the ventricular form of the venous pulse may appear, in spite of the sinus rhythm (see above).

2 *Nodal Rhythm* (*Fig* 37).—In nodal rhythm, the auricles and ventricles contract more or less simultaneously. Thus, auricular systole occurs during ventricular systole and when the *a–v* valves are closed. Therefore some of the blood is propelled upward to the jugular vein, and a large systolic pulsation of the jugular vein appears synchronous with each pulse beat.

3. *Incomplete A-V Block* (2:1, 3:1, *type, etc*) (*Fig.* 37) —With each pulse beat, the jugular veins show a systolic collapse, but since the auricles are beating faster than the ventricles, additional *a* waves can be seen during diastole, in the intervals between radial pulse beats By counting the *a* waves and the radial pulse, the exact degree of *a–v* block can frequently be determined Occasionally the Wenckebach type of *a–v* block (page 325) can be similarly diagnosed

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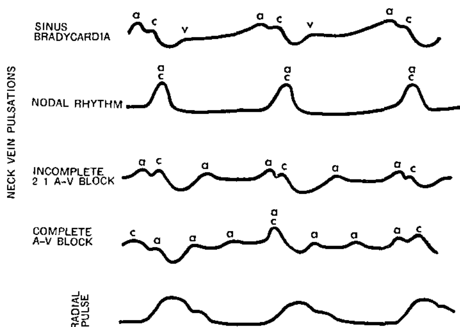


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Cardiac disease, especially mitral insufficiency and stenosis, on the other hand, can also produce abnormalities of the shape of the thorax. When mitral insufficiency and stenosis occur in young children, the forceful pulsation of a hypertrophied right ventricle causes a localized bulge of the precordium, between the sternum and the apex In addition, the left nipple is displaced upward and outward. A similar precordial bulging occurs in

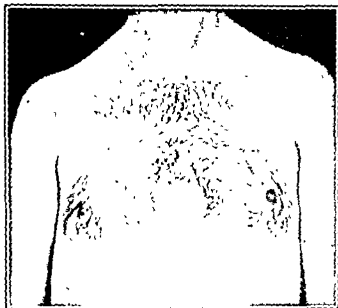


FIG 38.—Precordial bulging and outward displacement of the left nipple in a patient with right ventricular hypertrophy from childhood In this patient, the right ventricular hypertrophy was due to congenital heart disease (congenital pulmonary stenosis) rather than to rheumatic mitral stenosis

cases of congenital heart disease with enlargement of the right ventricle (Fig. 38). Rarely, pressure of a large left auricle on the vertebral column causes such marked distortion of the thorax that the posterior-anterior diameter of the thorax equals or exceeds the transverse diameter of the thorax.

Abnormal Pulsations of the Chest Wall.—Normal chest wall pulsations were described on page 35 Some of the common abnormal pulsations are

Abnormal Pulsations at the Base of the Heart.—A forcefully beating pulmonary artery can cause a slight systolic pulsation in the second left intercostal space normally. However, marked systolic pulsations here may occur in cases of patent ductus arteriosus, aneurism of the pulmonary artery, or any condition associated with a dilated pulmonary artery. Marked pulsa-

apneic periods usually last from ten to forty seconds, the hyperpneic periods from fifteen to fifty-five seconds In preterminal states, the apnea may last more than a minute. This can produce marked cyanosis, unconsciousness and even convulsive movements. During the hyperpneic periods, dyspnea may appear.

Variations in the blood pressure and pulse rate may occur with the respiratory variations, a decrease in blood pressure and slowing of the pulse occurring during the hyperpneic periods The pulse may not only slow, due to sinus bradycardia, but *a–v* dissociation, incomplete or complete *a–v* block and even cardiac standstill may occur during the hyperpneic periods These arrhythmias are due to vagal stimulation and may be abolished by atropine, which however, does not cause the Cheyne-Stokes respiration to disappear The vagal stimulation is mediated through the carotid sinus because manual stimulation of the carotid sinus in patients with Cheyne-Stokes respiration can precipitate these arrhythmias. (In Cheyne-Stokes respiration due to increased intracranial pressure, a decrease in blood pressure and a slowing of the pulse occur during the apneic periods).

Cheyne-Stokes respiration is due to a combination of a decreased carbon dioxide content of the blood and a depressed and erratic medullary respiratory center During the periods of hyperpnea, the hyperventilation washes out a large quantity of carbon dioxide from the body, and the blood level of carbon dioxide falls. Because of this, the respiratory center, which is very sensitive to fluctuations in carbon dioxide, is not stimulated, and apnea results During the period of apnea, the carbon dioxide level of the blood rises, the respiratory center is again stimulated, and hyperpnea reappears.

A form of Cheyne-Stokes respiration may also occur in patients with complete *a–v* block who develop cardiac standstill (the Adams-Stokes syndrome) During the intervals of cardiac standstill, anoxia of the respiratory center occurs but respiration continues, and the carbon dioxide content of the blood decreases When the heart begins to beat again, blood containing the low carbon dioxide content is pumped to the respiratory center, which is unresponsive so that apnea may appear If the apnea persists, convulsive movements may develop, in spite of the fact that the heart has begun to beat.

Although Cheyne-Stokes respiration can occur in normal persons during sleep or at high altitudes, it is a serious sign when it occurs during the waking hours. It occurs with various forms of heart disease, especially in hypertensive heart disease, left-sided failure and coronary artery disease It also occurs in cerebral arteriosclerosis, and in conditions with increased intracranial pressure, and can be produced by morphine. The presence of Cheyne-Stokes respiration often indicates that death is near, but patients may recover.

The most effective treatment of Cheyne-Stokes respiration is aminophylline, 0.5 gram (7½ grains) intramuscularly (a 2 cc. ampoule), or intravenously (a 10 cc. ampoule). The dose can be repeated several times daily. The inhalation of carbon dioxide is also effective.

Abnormal Shape of the Thorax.—The normal shape of the thorax was described on page 35. Recognition of an abnormality such as kyphoscoliosis is important because it can cause murmurs, distortion of the cardiac silhou-

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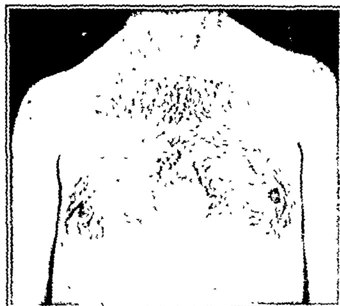


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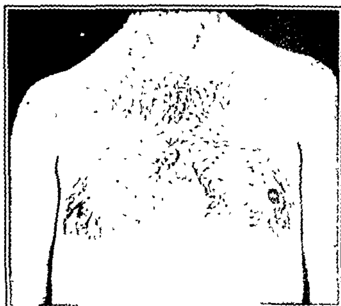


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apneic periods usually last from ten to forty seconds, the hyperpneic periods *from fifteen to fifty-five seconds. In preterminal states, the apnea may last* more than a minute. This can produce marked cyanosis, unconsciousness and even convulsive movements. During the hyperpneic periods, dyspnea may appear.

Variations in the blood pressure and pulse rate may occur with the respiratory variations, a decrease in blood pressure and slowing of the pulse occurring during the hyperpneic periods. The pulse may not only slow, due to sinus bradycardia, but *a–v* dissociation, incomplete or complete *a–v* block and even cardiac standstill may occur during the hyperpneic periods. These arrhythmias are due to vagal stimulation and may be abolished by atropine, which however, does not cause the Cheyne-Stokes respiration to disappear. The vagal stimulation is mediated through the carotid sinus because manual stimulation of the carotid sinus in patients with Cheyne-Stokes respiration can precipitate these arrhythmias. (In Cheyne-Stokes respiration due to increased intracranial pressure, a decrease in blood pressure and a slowing of the pulse occur during the apneic periods).

Cheyne-Stokes respiration is due to a combination of a decreased carbon dioxide content of the blood and a depressed and erratic medullary respiratory center. During the periods of hyperpnea, the hyperventilation washes out a large quantity of carbon dioxide from the body, and the blood level of carbon dioxide falls. Because of this, the respiratory center, which is very sensitive to fluctuations in carbon dioxide, is not stimulated, and apnea results. During the period of apnea, the carbon dioxide level of the blood rises, the respiratory center is again stimulated, and hyperpnea reappears.

A form of Cheyne-Stokes respiration may also occur in patients with complete *a–v* block who develop cardiac standstill (the Adams-Stokes syndrome). During the intervals of cardiac standstill, anoxia of the respiratory center occurs but respiration continues, and the carbon dioxide content of the blood decreases. When the heart begins to beat again, blood containing the low carbon dioxide content is pumped to the respiratory center, which is unresponsive so that apnea may appear. If the apnea persists, convulsive movements may develop, in spite of the fact that the heart has begun to beat.

Although Cheyne-Stokes respiration can occur in normal persons during sleep or at high altitudes, it is a serious sign when it occurs during the waking hours. It occurs with various forms of heart disease, especially in hypertensive heart disease, left-sided failure and coronary artery disease. It also occurs in cerebral arteriosclerosis, and in conditions with increased intracranial pressure, and can be produced by morphine. The presence of Cheyne-Stokes respiration often indicates that death is near, but patients may recover.

The most effective treatment of Cheyne-Stokes respiration is aminophylline, 0.5 gram ($7\frac{1}{2}$ grains) intramuscularly (a 2 cc. ampoule), or intravenously (a 10 cc. ampoule). The dose can be repeated several times daily. The inhalation of carbon dioxide is also effective.

Abnormal Shape of the Thorax.—The *normal shape* of the thorax was described on page 35. Recognition of an abnormality such as kyphoscoliosis is important because it can cause murmurs, distortion of the cardiac silhou-

Broadbent's sign can be produced in the following ways:

1. In adhesive pericarditis (page 649), or in constrictive pericarditis (page 650), the heart and pericardium may be adherent not only to the central tendon of the diaphragm, but to a large area of its muscular portion. With systole, therefore, the diaphragm and the lower ribs and costal cartilages are pulled inward

2. In tricuspid insufficiency and in aortic insufficiency, systole produces a marked decrease in the volume of the heart, and a decrease in intrathoracic pressure, which causes the retraction of the chest wall.

Abnormal Pulsations Due to Coarctation of the Aorta.—With coarctation, marked pulsation of the intercostal arteries, especially near the angle of the scapula may occur. The scapular pulsations can be made more visible by having the patient bend forward and pull his scapulae laterally

Abnormal Epigastric Pulsations—The normal epigastric pulsations were described on page 37. A marked systolic pulsation in the epigastrium may occur with pulsation of the liver, in which case it is diffuse (see page 150), or may be transmitted from an hypertrophied right ventricle In such a case, a marked systolic pulsation of the left lower sternal border is also present. An epigastric systolic pulsation may also be transmitted from the abdominal aorta Here it is localized to the epigastrium, and with pressure with the fist, the aortic pulsations become more prominent.

Rarely, an abnormal epigastric pulsation may be due to a diverticulum of the left ventricle.

Thrills.—A thrill is the palpable equivalent of a murmur, and is produced in the same way as the murmur it represents. Loud murmurs are frequently associated with thrills, soft murmurs usually occur without thrills, although exceptions to this statement are frequent Because the hand is not sensitive to high-pitched vibrations, and the ear is not sensitive to low-pitched vibrations, a thrill may be present without an audible murmur, and vice versa This is particularly noticable in cases of mitral stenosis, where a marked diastolic thrill may be present with an almost inaudible diastolic murmur For this reason, the search for thrills is valuable. Thrills are also useful because they are usually more localized, and are not transmitted as far as murmurs. The presence of a thrill at the apex or base therefore helps localize the site of origin of a murmur When a thrill is sought, the palm should be lightly placed on the precordium Pressure obliterates the thrill.

The significance of a thrill is that it indicates the presence of a murmur or of a condition conducive to murmur formation. Although it is theoretically possible for a thrill to occur with a loud normal murmur, the presence of a thrill in association with a murmur should be considered a sign that the murmur is abnormal. However, the presence of a thrill does not necessarily indicate that an organic lesion is present. For example, a diastolic apical thrill can occur with functional or organic mitral stenosis.

Thrills are common in stenotic valvular lesions, such as aortic stenosis and mitral stenosis, but relatively rare in cases of valvular insufficiency, either aortic, mitral or pulmonary, although they do occur here In this connection, the rough systolic apical thrust of a rapidly beating normal heart in a thin-chested person should not be mistaken for a thrill whose vibrations are rapid and fine, like the purring of a cat.

tions at the base, to the right of the sternum, should arouse suspicion of an aortic aneurism.

A forceful pulsation in the suprasternal notch may be produced by a forcibly beating or dilated aorta. Palpation here may disclose a diastolic shock, due to forceful closure of the aortic valve. Palpation over the pulmonary area may reveal a diastolic shock due to forceful closure of the pulmonary valve. This is not necessarily abnormal.

Abnormal Pulsations in the Sternal Region.—A forceful systolic pulsation to the left of the sternum at about the level of the fourth intercostal space, indicates a hypertrophied right ventricle. It can best be noted by placing the thenar eminence of the palm of the hand over this region. When right ventricular hypertrophy occurs with tricuspid insufficiency, there may be systolic retraction of this region (see under Broadbent's Sign, below).

Abnormal Pulsations at the Apex.—Hypertrophy and dilatation of the left ventricle can frequently be determined from the character of the apical impulse. Normally, in adults, the apical impulse is not prominent, except in very thin people. A prominent apical impulse in an adult, especially in the lying position, is suggestive of left ventricular hypertrophy. Hypertrophy is determined by finding (1) the apical impulse displaced outside the left midclavicular line, (2) an enlarged area of the apex beat which can be covered only by two or more fingers, (3) a forceful impulse which imparts a sense of hardness and resistance to the finger. Occasionally the impact of a hypertrophied left ventricle is so forceful that the left side of the chest moves out and the sternal region moves inward, giving a rocking appearance to the entire chest wall. Dilatation of the heart on the other hand, is characterized by a wide, diffuse apical impulse, outside the midclavicular line.

The presence of a diastolic gallop or of an accentuated third heart sound may produce a double pulsation at the apex. The systolic pulsation is the normal apical impulse. The diastolic pulsation is due to the vibrations of the ventricular wall in diastole which produce the gallop sound (see page 159). A double systolic pulsation may occur in cases of bundle branch block (page 374).

Abnormal Pulsations in Ventricular Aneurism.—The following physical signs may occur with a ventricular aneurism:

1. The apical impulse may be felt well within the outer limits of cardiac dullness.

2. Two apical impulses may be palpated, one near the sternum. This extra impulse may begin before, may last longer, and may be more marked than the regular apical impulse.

3. A poor, dull, first heart sound at the apex may be present, far out of proportion to the apparently forceful apical impulse.

Broadbent's Sign.—Broadbent first described a systolic retraction of some of the lower ribs on the lateral or posterior aspect of the thorax as a sign of constrictive pericarditis. A similar diffuse systolic depression of the precordium, involving the ribs and soft tissues, over several intercostal spaces has also been noted in tricuspid insufficiency and in aortic insufficiency. However, when Broadbent's sign is associated with a pulsus paradoxicus (page 141), a diagnosis of constrictive pericarditis is justified.

Pericardial effusion can also cause a marked increase in cardiac flatness. The following physical signs are also present: an obtuse cardiohepatic angle in the fifth right intercostal space near the sternum (Rotch's sign) and flatness under the sternum at the level of the fourth and third intercostal spaces. However, I have observed all these signs in the absence of pericardial effusion, when marked enlargement of the right ventricle and right and left auricles were present However, when pericardial effusion is present, these signs are not only present, but, in addition, the transition from pulmonary resonance to flatness is very sharp, whereas, with enlargement of the heart, the resonance changes to dullness, and within this is found the flat area (Fig 39). Another sign of pericardial effusion is the presence of a palpable apical impulse well within the point where the cardiac flatness appears.

Abnormal Cardiac Dullness Due to Generalized Displacement of the Heart.—In pulmonary fibrosis or massive atelectasis this occurs toward the affected side of the chest Pneumothorax or massive pleural effusion may displace the heart toward the contralateral side to a moderate degree Moderate displacement of the heart may occur with a funnel chest.

ABNORMAL HEART SOUNDS

Distant Heart Sounds.—These occur normally in obese people and in patients with emphysema. Abnormal conditions such as pericardial effusion, and especially myocardial infarction can also cause a marked decrease in the intensity of both heart sounds, the sounds gradually becoming louder as the effusion subsides or the infarct heals However, after infarction, in some cases, the sounds do not return to their original intensity

Loud Heart Sounds.—These occur in thin-chested people, especially if the heart is beating rapidly Rarely the heart sounds are heard at a distance from the chest wall. This occurs in left pneumothorax, pneumopericardium, and occasionally after rupture of a valve cusp, chorda tendinea, or after myocardial infarction when an infarcted papillary muscle allows the mitral valve to close very abruptly.

Abnormalities of the First Heart Sound.—The intensity of the first heart sound is determined at the apex A weak first heart sound with a normal second sound has no significance A loud or snapping first sound with a normal second sound occurs when the ventricles contract abruptly and rapidly as in exercise, anemia, hyperthyroidism, *etc* More important is its appearance in mitral stenosis

Variations in the intensity of the first heart sound can be explained in the following way: Since the first heart sound is produced principally by the closure of the *a–v* valves, the position of the *a–v* valves at the moment of ventricular systole is important. During auricular systole, the valves are driven deep in the ventricles, floating upward at the end of auricular systole. Thus, if ventricular systole begins soon after auricular systole, the valves will be caught at a low position, and the snap that results as they are thrown upward with ventricular systole will be louder than would occur alter when the *a–v* valves had risen.

ABNORMAL AREAS OF CARDIAC DULLNESS AND FLATNESS

The normal areas of cardiac dullness and flatness were described on page 38.

Abnormal Dullness at the Base of the Heart.—Abnormal dullness in the first or second intercostal space to the right or left of the sternum occurs with aortic dilatation or aneurism of the ascending aorta, mediastinal lesions, even pericardial effusion. Dullness to the right of the sternum is occasionally due to a right aortic arch. Dullness to the left of the sternum may also occur in patent ductus arteriosus, the dilated pulmonary artery being lifted up by the ductus. However, I would hardly want to make a diagnosis of a patent ductus on the basis of this finding alone. Dullness in the third left intercostal space is usually due to mitral stenosis, the large right ventricle pushing the pulmonary artery outward. However, dullness here may occur with any condition associated with a dilated pulmonary artery.

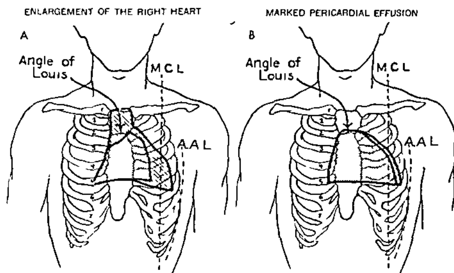


FIG. 39.—*A*, Abnormal area of percussion due to enlargement of the right ventricle and auricle. *B*, Abnormal area of percussion due to pericardial effusion. Striped areas indicate cardiac dullness. Stippled areas indicate cardiac flatness. See text.

Abnormal Dullness at the Apex.—Dullness to the left of the left midclavicular line in the fourth, fifth or sixth intercostal space is due to enlargement of the right or left ventricle or both, or to marked pericardial effusion or left pleural effusion.

Abnormal Dullness at the Right Sternal Area.—Dullness to the right of the sternum in the fourth or fifth intercostal spaces is caused by enlargement of the right or left auricle or both, or pericardial or right pleural effusion.

Abnormal Cardiac Flatness.—When enlargement of the right ventricle is present, the area of cardiac flatness enlarges upward and to the right and left of the sternum. When the right or left auricle or both are enlarged, marked flatness is present to the right of the sternum, even in the third and fourth intercostal spaces (Fig. 39, *A*).

in cases of hypertension of the pulmonary circulation as in mitral stenosis, and chronic pulmonary disease, and a loud aortic second sound occurs particularly with hypertensive cardiovascular disease However, I have never paid too much attention to these relations because rotation of the heart in a clockwise direction will bring the aorta and a loud aortic second sound to the left of the sternum, even in the absence of pulmonary hypertension Similarly, in a case of aortic stenosis, where the aortic second sound should be faint or absent, counterclockwise rotation of the heart brings the pulmonary artery to the right, and a good second sound can be heard in the aortic valve area

Reduplication of the pulmonary second sound frequently occurs in mitral stenosis, but also occurs normally and in many cases with pulmonary hypertension

In aortic valve disease where an early diastolic murmur occurs, the aortic second sound may be masked

The Opening Snap of the Mitral Valve.—This is an important sign of mitral stenosis, because when it is present, the diagnosis of mitral stenosis can be made even if a presystolic or diastolic murmur is absent It is a short, sharp snap or click heard best in the third or fourth intercostal space between sternum and apex It is heard distinct from the second sound, *which it follows, unlike a split second sound, with which it is frequently* confused and which has no clinical significance It is best heard when the heart rate is rapid

It can be differentiated phonocardiographically from both a split second sound and a third sound or diastolic gallop because the opening snap occurs simultaneously with the peak of the *v* wave of the jugular phlebogram, (when the mitral valve opens) The split second sound occurs with the closure of the semilunar valves, before the mitral valve opens, and therefore appears before the peak of the *v* wave The third sound or a diastolic gallop occurs after the opening of the *a–v* valves and during the stage of rapid ventricular filling and appears simultaneously with the descending limb of the *v* wave (see figure 4, page 52)

The opening snap is significant because it occurs only with a scarred and fibrosed mitral valve.

The Third Heart Sound and Gallop Rhythm —On page 40, I pointed out that with the rapid inflow of blood into the ventricles in early diastole, a third heart sound occurs in children and young adults When this sound is heard in patients with left-sided heart failure, the sequence of the first, *second,* and third sounds is called gallop rhythm

The gallop sound is usually dull and low-pitched and is heard best by having the patient lie about midway between the supine and left lateral positions. Its phonetic equivalent is *lub* dub da, the three sounds seeming to be equidistant from each other The gallop is greatly increased by acceleration of the heart rate, and when the rate falls much below 100, it may disappear even though all the conditions for its presence still remain

The gallop may not only be heard but also may be palpated and even seen over the apical region as a strong precordial shock during diastole. In the presence of right-sided heart failure, gallop has been described over the xiphoid region. Gallop rhythm usually disappears when compensation is restored, but in some cases it may persist even for years.

In mitral stenosis, a low position of the *a–v* valves occurs because the passage of blood from auricles to ventricles through the stenosed valve is difficult, and ventricular filling is still incomplete and the valves are still descended at the moment of ventricular systole. In anemia, exertion, *etc.*, the ventricular rate is rapid and the duration of diastole decreased, so that at the beginning of ventricular systole the *a–v* valves are lower than at a slow rate

The position of the *a–v* valves explains the variations in the first heart sound associated with many of the cardiac arrhythmias. For example, the longer the *P–R* interval of the electrocardiogram in a case of first degree *a–v* block, the lower the intensity of the first sound, because a long *P–R* interval is associated with a long interval between auricular and ventricular systole Thus, in cases of acute rheumatic fever, where daily variations in the *P–R* interval may occur, the changing intensity of the first sound has been erroneously ascribed to myocarditis. Similar variations in the first sound, however, occur in normal people who show daily variations in the *P–R* interval

Variations in the intensity of the first sound also occur in complete *a–v* block, and when the *P–R* interval is short, an explosive first sound, called a *cannon sound*, may occur. So characteristic are the variations in the *intensity of the first heart sound in complete a–v block that their presence* in a patient with a slow regular ventricular rate is in itself suggestive of complete *a–v* block.

A similar change in the intensity of the first heart sound can occur in patients with a rapid heart rate, as in ventricular tachycardia, where the auricles usually beat at a slower rate, independently of the ventricles, and in auricular flutter with an irregular ventricular rhythm, and in auricular tachycardia with variations in the *P–R* interval

When the *P–R* interval is short, the auricular component of the first heart sound adds to the intensity of the first sound. However, this factor is not too important because in cases of complete *a–v* block, the first sound is not extremely loud nor do the cannon sounds appear when the auricles and ventricles contract simultaneously. Similarly, the first heart sound is not abnormally loud in the Wolff-Parkinson-White syndrome even though the *P–R* interval is very short

Abnormalities of the Second Heart Sound.—The intensity of the second sound is determined at the base of the heart in the second intercostal space. A loud, booming second sound is characteristic of hypertensive cardiovascular disease. It is usually heard best at the aortic valve area, to the right of the sternum, but may be heard at the pulmonary valve area, to the left of the sternum. The exact cause of this booming sound is unknown, because it frequently persists even when the blood pressure drops to normal, either spontaneously, with medication, during decompensation, after myocardial infarction, *etc.* As a matter of fact, when I find a booming second sound in the presence of a low blood pressure in an apparently healthy person, I suspect an old myocardial infarct.

Much has been written about the relative intensity of the second sound at the right and left borders of the sternum. The normal relations were described on page 41. In adults, a loud pulmonary second sound occurs

in cases of hypertension of the pulmonary circulation as in mitral stenosis, and chronic pulmonary disease, and a loud aortic second sound occurs particularly with hypertensive cardiovascular disease. However, I have never paid too much attention to these relations because rotation of the heart in a clockwise direction will bring the aorta and a loud aortic second sound to the left of the sternum, even in the absence of pulmonary hypertension. Similarly, in a case of aortic stenosis, where the aortic second sound should be faint or absent, counterclockwise rotation of the heart brings the pulmonary artery to the right, and a good second sound can be heard in the aortic valve area.

Reduplication of the pulmonary second sound frequently occurs in mitral stenosis, but also occurs normally and in many cases with pulmonary hypertension.

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The gallop may not only be heard but also may be palpated and even seen over the apical region as a strong precordial shock during diastole In the presence of right-sided heart failure, gallop has been described over the xiphoid region. Gallop rhythm usually disappears when compensation is restored, but in some cases it may persist even for years.

When gallop rhythm is studied phonocardiographically, three different types can be recognized:

1 **Protodiastolic Gallop, or Rapid Filling Gallop.**—This was just described. It is due to an audible third heart sound occurring during the phase of rapid ventricular filling The gallop occurs on the descending limb of the jugular *v* wave, and coincides with the *ri* wave of the apex cardiogram (page 53) The term "protodiastolic" as used for this gallop is different from the term "protodiastolic" used in connection with the cardiac cycle, (page 40).

2 **Presystolic Gallop.**—The diagnosis is made when the extra sound occurs during auricular systole. The sound occurs simultaneously with the jugular *a* wave

3 **Summation Gallop.**—This occurs when the extra sounds due to rapid ventricular filling and auricular systole coincide. This is usually brought about by tachycardia which shortens diastole. In such a case, the jugular *a* wave tends to merge with the *v* wave, and the sound vibrations of the protodiastolic and presystolic gallops coincide, producing a loud sound

By simple auscultation it is practically impossible to specify to which type of gallop a given case corresponds, and from a clinical point of view, unnecessary, because the significance of each of the types is the same Rarely, if both protodiastolic and presystolic gallops are present, four heart sounds can be heard with each heart beat.

OTHER ABNORMAL HEART SOUNDS

The Protodiastolic Pericardiac Vibration.—This sometimes occurs with calcification of the pericardium It also is related to the third heart sound because it occurs during the peak of ventricular filling. It is a fairly sharp, high- pitched sound, due to the impact of the heart against the calcified pericardium.

Pericardial Knock—This is an extremely loud knocking, popping or snapping sound, heard only in systole, especially in the left lateral position, and sometimes heard at a distance from the patient It occurs with left-sided pneumothorax and partial collapse of the lung It has no relation to pericardial pathology, its name notwithstanding.

Sounds Heard in Mediastinal Emphysema.—A crunching, crepitating sound, similar to the pericardial knock, but systolic or diastolic, is heard *along the left sternal border in cases of spontaneous or traumatic mediastinal* emphysema.

Water-Wheel Murmur.—This is a churning or splashing noise which occasionally occurs if there is air and fluid in the pericardium (hydropneumopericardium) It also occurs after venous air embolism when air is trapped in the right ventricular cavity. Sometimes the murmur is so loud that it can be heard without a stethoscope.

Splashing Sounds.—Splashing sounds may occur with each heart beat when the heart is overactive, and there is gas and fluid in the stomach. These sounds have no significance.

Pericardial Friction Rubs.—These are rough, rasping and leathery sounds either systolic and diastolic, sometimes only systolic, but never diastolic

alone, due to the sliding of inflamed epicardium against the parietal pericardium in acute pericarditis They may be heard over the left sternal border, or be widely transmitted over the entire precordium and back The rub sometimes can also be palpated as a thrill When the rub is soft, it can be easily mistaken for a murmur.

The rub seems superficial, close to the ear and is intensified when the stethoscope bell is pressed against the chest Marked pressure with the stethoscope may cause the intensity of the rub to decrease The rub is usually fleeting and frequently audible for only a few hours, but in some cases persists for days It occurs with both fibrinous pericarditis and pericarditis with effusion

Occasionally, a rough, grating systolic murmur, almost identical with a friction rub, occurs at the base, especially over the sternum and the second intercostal space, in cases of hyperthyroidism, and acute cor pulmonale and in the absence of pericarditis It is heard best at the end of a deep expiration, and is obscured by inspiration. It is probably of pleuro-pericardial origin.

Auricular Sounds.—A loud auricular sound can produce a presystolic gallop (page 160) or give the appearance of a split first sound (page 41) Faint, isolated auricular sounds also occur during ventricular diastole in cases of incomplete and complete *a-v* block They are heard best at the left border of the sternum and at the apex, using a bell stethoscope

ABNORMAL MURMURS

The mechanism of murmur production and a description of normal murmurs were described on page 43 Here I shall describe the characteristics of some of the more common abnormal murmurs In this connection one should remember that diastolic murmurs are usually softer than systolic murmurs and may be difficult to hear This is especially true of the diastolic apical murmur of mitral stenosis

Abnormal Murmurs at the Aortic Area

Abnormal Aortic Systolic Murmurs.—A systolic murmur loudest at the second right intercostal space usually has its origin in the aortic valve Such murmurs are frequently transmitted to the neck, and along the left sternal border toward the apex. The most common cause of a systolic aortic murmur is essential hypertension where the murmur is probably due to the forceful ejection of blood into the aorta A booming aortic second sound is usually also present Aortic stenosis, and rarely congenital subaortic stenosis also produce a systolic aortic murmur With aortic stenosis, the murmur may mask the first sound and frequently but not necessarily is associated with a diminished or absent aortic second sound The murmur of aortic stenosis is harsh and rough and usually but not necessarily is accompanied by a thrill The murmur may be faintly audible or very loud In some cases it can be heard without a stethoscope When it is faint, it is best heard by having the patient sit up, bend forward, and hold his breath after exhaling deeply.

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The mechanism of murmur production and a description of normal murmurs were described on page 43. Here I shall describe the characteristics of some of the more common abnormal murmurs. In this connection one should remember that diastolic murmurs are usually softer than systolic murmurs and may be difficult to hear. This is especially true of the diastolic apical murmur of mitral stenosis.

Abnormal Murmurs at the Aortic Area

Abnormal Aortic Systolic Murmurs.—A systolic murmur loudest at the second right intercostal space usually has its origin in the aortic valve. Such murmurs are frequently transmitted to the neck, and along the left sternal border toward the apex. The most common cause of a systolic aortic murmur is essential hypertension where the murmur is probably due to the forceful ejection of blood into the aorta. A booming aortic second sound is usually also present. Aortic stenosis, and rarely congenital subaortic stenosis also produce a systolic aortic murmur. With aortic stenosis, the murmur may mask the first sound and frequently but not necessarily is associated with a diminished or absent aortic second sound. The murmur of aortic stenosis is harsh and rough and usually but not necessarily is accompanied by a thrill. The murmur may be faintly audible or very loud. In some cases it can be heard without a stethoscope. When it is faint, it is best heard by having the patient sit up, bend forward, and hold his breath after exhaling deeply.

Occasionally, the murmur of aortic stenosis may be high pitched and squeaking.

Differential Diagnosis of Aortic Systolic Murmurs.—When a harsh systolic aortic murmur occurs, transmitted to the neck, associated with a thrill and an absent aortic second sound, the diagnosis of aortic stenosis is justified. However, the majority of cases of aortic stenosis do not show these findings, and in most cases an etiological diagnosis *of an aortic systolic* murmur cannot be made from the characteristics of the murmur alone.

Aortic insufficiency is also often accompanied by a systolic aortic murmur in association with a characteristic diastolic murmur and peripheral signs of aortic insufficiency. The systolic murmur in such cases is due to the forceful ejection of blood into the aorta. However, one should not forget that patients with pure aortic stenosis or subaortic stenosis may have systolic and diastolic aortic murmurs In such cases, the peripheral signs of aortic insufficiency are absent, but the exact cause of the diastolic murmur here is not known Coarctation of the aorta also produces a systolic murmur at the aortic area. This murmur is not only transmitted to the neck vessels but to the back, where it is as loud or almost as loud as the murmur anteriorly. This is an important sign of coarctation (see page 455). A dissecting aneurism of the aorta may also produce an aortic systolic murmur.

Abnormal Aortic Diastolic Murmurs.—A diastolic murmur at the aortic area can occur in the following ways:

1 *Organic Aortic Insufficiency* (*Syphilitic or Rheumatic*) —The murmur is blowing in character, occasionally musical, usually high-pitched, but may be soft or loud It may or may not mask the second sound. When it is soft, it can be heard better with the patient leaning forward, and by using the Bowles stethoscope or the naked ear When the murmur is due to syphilitic aortic insufficiency, it is often very harsh, loud, may sound like *the buzzing of a saw, and may even be audible without the stethoscope* The murmur of rheumatic aortic insufficiency is usually softer and lower pitched The musical murmur of syphilitic aortic insufficiency is sometimes due to eventration of one of the aortic cusps

The murmur is transmitted along the left sternal border toward the apex. When it is due to rheumatic aortic insufficiency, it is usually heard best in the third left interspace, and not in the aortic area, contrary to the murmur of syphilitic aortic insufficiency. There are several reasons for this: In rheumatic heart disease, clockwise rotation of the heart is common. This rotates the aorta toward the left. In syphilitic aortic insufficiency, there is usually marked dilatation of the aorta, which extends beneath the sternum toward the right. In addition, massive left ventricular enlargement is often present, and with it counterclockwise rotation, which rotates the aorta to the right However, it may be impossible in a particular case, to determine from the murmur alone, whether the aortic insufficiency is of rheumatic or syphilitic origin.

2. *Functional Aortic Insufficiency.*—This can occur in dissecting aneurism of the aorta (page 661), and in dynamic dilatation of the aorta (page 536).

Other conditions can also produce an aortic diastolic murmur. I mentioned above that it appears in a fair proportion of patients with pure

aortic stenosis, proven at autopsy, and in cases of subaortic stenosis. In both these conditions, the peripheral signs of aortic insufficiency are missing. Dissecting aneurism of the aorta can also produce systolic and diastolic murmurs which completely mimic those of aortic insufficiency, including the peripheral signs. In such cases, the aortic ring is probably deformed by the dissecting column of blood.

Differential Diagnosis of Aortic Diastolic Murmurs.—Some of the differences between syphilitic and rheumatic aortic insufficiency have been mentioned above. Other points of distinction are the following: rheumatic aortic insufficiency is seen in the younger age groups, syphilitic aortic insufficiency in older people. Frequently in rheumatic aortic insufficiency, precordial prominence or marked displacement of the left nipple is present, indicating that the heart disease began in childhood In most cases of syphilitic aortic insufficiency, the Wassermann test or one of its modifications is positive, but it is very possible for a patient with rheumatic heart disease to have coincidental syphilis When aortic insufficiency and stenosis of rheumatic origin are present, the systolic and diastolic murmurs may simulate those of syphilitic aortic insufficiency, but the pulse pressure is small, unlike the large pulse pressure of syphilitic aortic insufficiency. In addition, in cases of rheumatic aortic insufficiency, there is often involvement of the mitral valve resulting in left auricular enlargement, whereas in syphilitic aortic insufficiency, the enlargement is predominantely left ventricular A presystolic murmur may occur at the apex in rheumatic aortic insufficiency if mitral stenosis is also present, but it may occur in isolated aortic insufficiency as a sign of the Austin Flint murmur (page 168)

The differential diagnosis between organic and functional aortic insufficiency may be impossible unless the murmurs disappear as cardiac compensation returns. Peripheral signs of aortic insufficiency are absent in aortic and subaortic stenosis However, they may be absent in a case of isolated aortic insufficiency if the valve is not severely damaged

Abnormal Murmurs at the Pulmonary Area

Abnormal Pulmonary Systolic Murmurs.—A systolic murmur heard best at the second or third left intercostal space is often normal, as I pointed out on page 44 Abnormal conditions that can cause it are:

1 Dilatation of the pulmonary artery. This can be due to congenital idiopathic dilatation of the pulmonary artery, aneurism of the pulmonary artery, *dilatation secondary to mitral stenosis, or associated with inter*-auricular septal defects, the Eisenmenger complex, chronic pulmonary disease, *etc*

2 Conditions associated with pulmonary stenosis, such as congenital pulmonary stenosis, the tetralogy of Fallot, *etc*

The murmur of the tetralogy of Fallot has been described as sounding close to the sternum, harsh, lasting throughout systole, and giving the impression of a squirt, rather than the blowing murmur of acquired heart disease. However, in my experience, this does not always occur.

3. Transmission of an aortic murmur to the pulmonary area.

4 In infants and children, a patent ductus arteriosus may occur with only a systolic murmur at the pulmonary area.

Occasionally, the murmur of aortic stenosis may be high pitched and squeaking

Differential Diagnosis of Aortic Systolic Murmurs.—When a harsh systolic aortic murmur occurs, transmitted to the neck, associated with a thrill and an absent aortic second sound, the diagnosis of aortic stenosis is justified However, the majority of cases of aortic stenosis do not show these findings, and in most cases an etiological diagnosis of an aortic systolic murmur cannot be made from the characteristics of the murmur alone

Aortic insufficiency is also often accompanied by a systolic aortic murmur in association with a characteristic diastolic murmur and peripheral signs of aortic insufficiency. The systolic murmur in such cases is due to the forceful ejection of blood into the aorta. However, one should not forget that patients with pure aortic stenosis or subaortic stenosis may have systolic and diastolic aortic murmurs In such cases, the peripheral signs of aortic insufficiency are absent, but the exact cause of the diastolic murmur here is not known Coarctation of the aorta also produces a systolic murmur at the aortic area This murmur is not only transmitted to the neck vessels but to the back, where it is as loud or almost as loud as the murmur anteriorly. This is an important sign of coarctation (see page 455). A dissecting aneurism of the aorta may also produce an aortic systolic murmur

Abnormal Aortic Diastolic Murmurs.—A diastolic murmur at the aortic area can occur in the following ways:

1. *Organic Aortic Insufficiency (Syphilitic or Rheumatic).*—The murmur is blowing in character, occasionally musical, usually high-pitched, but may be soft or loud. It may or may not mask the second sound. When it is soft, it can be heard better with the patient leaning forward, and by using the Bowles stethoscope or the naked ear When the murmur is due to syphilitic aortic insufficiency, it is often very harsh, loud, may sound like the buzzing of a saw, and may even be audible without the stethoscope The murmur of rheumatic aortic insufficiency is usually softer and lower pitched. The musical murmur of syphilitic aortic insufficiency is sometimes due to eventration of one of the aortic cusps.

The murmur is transmitted along the left sternal border toward the apex When it is due to rheumatic aortic insufficiency, it is usually heard best in the third left interspace, and not in the aortic area, contrary to the murmur of syphilitic aortic insufficiency. There are several reasons for this: In rheumatic heart disease, clockwise rotation of the heart is common This rotates the aorta toward the left. In syphilitic aortic insufficiency, there is usually marked dilatation of the aorta, which extends beneath the sternum toward the right. In addition, massive left ventricular enlargement is often present, and with it counterclockwise rotation, which rotates the aorta to the right However, it may be impossible in a particular case, to determine from the murmur alone, whether the aortic insufficiency is of rheumatic or syphilitic origin.

2 *Functional Aortic Insufficiency.*—This can occur in dissecting aneurism of the aorta (page 661), and in dynamic dilatation of the aorta (page 536).

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aortic stenosis, proven at autopsy, and in cases of subaortic stenosis. In both these conditions, the peripheral signs of aortic insufficiency are missing. Dissecting aneurism of the aorta can also produce systolic and diastolic murmurs which completely mimic those of aortic insufficiency, including the peripheral signs. In such cases, the aortic ring is probably deformed by the dissecting column of blood.

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The differential diagnosis between organic and functional aortic insufficiency may be impossible unless the murmurs disappear as cardiac compensation returns. Peripheral signs of aortic insufficiency are absent in aortic and subaortic stenosis. However, they may be absent in a case of isolated aortic insufficiency if the valve is not severely damaged.

Abnormal Murmurs at the Pulmonary Area

Abnormal Pulmonary Systolic Murmurs.—A systolic murmur heard best at the second or third left intercostal space is often normal, as I pointed out on page 44. Abnormal conditions that can cause it are.

1. Dilatation of the pulmonary artery. This can be due to congenital idiopathic dilatation of the pulmonary artery, aneurism of the pulmonary artery, dilatation secondary to mitral stenosis, or associated with interauricular septal defects, the Eisenmenger complex, chronic pulmonary disease, *etc.*

2. Conditions associated with pulmonary stenosis, such as congenital pulmonary stenosis, the tetralogy of Fallot, *etc.*

The murmur of the tetralogy of Fallot has been described as sounding close to the sternum, harsh, lasting throughout systole, and giving the impression of a squirt, rather than the blowing murmur of acquired heart disease. However, in my experience, this does not always occur.

3. Transmission of an aortic murmur to the pulmonary area.

4. In infants and children, a patent ductus arteriosus may occur with only a systolic murmur at the pulmonary area.

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1 Dilatation of the pulmonary artery. This can be due to congenital idiopathic dilatation of the pulmonary artery, aneurism of the pulmonary artery, dilatation secondary to mitral stenosis, or associated with interauricular septal defects, the Eisenmenger complex, chronic pulmonary disease, *etc.*

2 Conditions associated with pulmonary stenosis, such as congenital pulmonary stenosis, the tetralogy of Fallot, *etc.*

The murmur of the tetralogy of Fallot has been described as sounding close to the sternum, harsh, lasting throughout systole, and giving the impression of a squirt, rather than the blowing murmur of acquired heart disease However, in my experience, this does not always occur.

3 Transmission of an aortic murmur to the pulmonary area.

4 In infants and children, a patent ductus arteriosus may occur with only a systolic murmur at the pulmonary area.

Differential Diagnosis of Pulmonary Systolic Murmurs.—The differentiation of an aortic systolic murmur transmitted to the pulmonary area, from a pulmonary systolic murmur may be difficult. However, loud pulmonary (and apical) systolic murmurs are transmitted clearly to the lung bases, whereas aortic murmurs are not

It may also be impossible to differentiate a normal from an abnormal pulmonary systolic murmur, by the characteristics of the murmur alone, although the normal pulmonary systolic murmur usually disappears in the upright position, whereas an abnormal pulmonary systolic murmur persists. The characteristics of the pulmonary second sound may be helpful in differential diagnosis In the tetralogy of Fallot and in pulmonary *stenosis, the pulmonary second sound is faint or absent, and is never split.* Occasionally, however, a prominent pulmonary second sound is present. This is actually transmitted from the aortic area. In both these conditions, a soft diastolic murmur may also be present at the pulmonary area.

Phonocardiographic analysis may help differentiate a normal pulmonary systolic murmur from the systolic murmur of pulmonary stenosis. The normal murmur is confined to mid-systole. The murmur of pulmonary stenosis occupies most of systole and continues almost up to the aortic second sound.

Abnormal Pulmonary Diastolic Murmurs.—Pulmonary diastolic murmurs can occur in the following ways

1. *Pulmonary Insufficiency*—This can be functional or organic. Organic pulmonary insufficiency is extremely rare, but functional pulmonary insufficiency is very common. When it occurs as a result of pulmonary artery dilatation secondary to mitral stenosis, the diastolic murmur is called a Graham Steell murmur. Functional pulmonary insufficiency also occurs with chronic pulmonary disease, left-sided heart failure, interauricular septal defects, idiopathic dilatation of the pulmonary artery, and the Eisenmenger complex In all these conditions, a systolic pulmonary murmur may also be present. Functional pulmonary insufficiency may also occur with a patent ductus arteriosus, and may be partially the cause of the diastolic murmur heard with a patent ductus.
2. Murmurs transmitted from the aortic area.
3. Congenital pulmonary stenosis is occasionally associated with a diastolic pulmonary murmur in addition to the systolic murmur. The cause of this is unknown

Differential Diagnosis of Pulmonary Diastolic Murmurs.—The murmurs of aortic insufficiency and pulmonary insufficiency may be identical on auscultation. Differentiation is possible, using the following criteria:

1. The aortic diastolic murmur is usually louder than the pulmonary, and is heard better in the third left intercostal space, unlike the pulmonary, which is more marked in the second left intercostal space.
2. The aortic murmur is transmitted to the neck, unlike most pulmonary diastolic murmurs. An exception occurs in patent ductus arteriosus and an aortic-pulmonary fistula
3. When the murmur is loud and due to aortic insufficiency, peripheral signs, such as the collapsing pulse, *etc*, are present. When the diastolic murmur is loud and due to pulmonary insufficiency, the pulmonary second

sound is accentuated, and on fluoroscopy a prominent pulmonary artery segment is present along with marked pulsations of the hilar vessels

Continuous Murmurs at the Base of the Heart

The most outstanding continuous murmur at the base of the heart is that due to a patent ductus arteriosus It is characterized by a continuous loud, harsh, not blowing machinery or humming-top murmur. A peculiarity often noted is that the murmur appears to become louder during the latter part of systole, enveloping the second sound, and then continuing with decreasing intensity during diastole. The murmur is heard best in the first and second left intercostal spaces, near the sternum. It is transmitted to the neck vessels It is usually associated with a systolic thrill and with visible pulsations in the second left intercostal space.

A similar continuous murmur occurs in a congenital aortic-pulmonary fistula, and a continuous murmur may appear in cases of the tetralogy of Fallot, due to blood rushing through a dilated collateral bronchial artery. A continuous murmur at the base may also occur after rupture of an aneurism of the aorta into the pulmonary artery, the superior vena cava, the right auricle or right ventricle Occasionally a continuous venous hum is transmitted along the base of the heart from the neck veins

Abnormal Murmurs Along the Sternal Border

Aortic and pulmonary murmurs are often transmitted along the left sternal border, and mitral murmurs can also be heard here Uncomplicated interventricular septal defects can produce a rough systolic murmur and thrill in the third or fourth intercostal space along the left sternal border, but it is my impression that the cause of such a murmur is much more frequently a subaortic stenosis

Tricuspid murmurs are theoretically heard at the xiphoid process and the fourth and fifth intercostal spaces to the right of the sternum. The systolic murmur of tricuspid insufficiency is extremely difficult to diagnose, and in most cases of tricuspid insufficiency, no murmur is heard. Sometimes the murmur can be intensified or brought out by having the patient take a deep breath and hold it. A mitral murmur, transmitted to the sternum, on the other hand will decrease in intensity with this maneuver, which is based on the fact that inspiration increases the blood flow into and through the right heart Most soft systolic murmurs heard along the the left sternal border are normal

In cases of tricuspid stenosis, a diastolic or presystolic murmur may appear Since most cases of tricuspid stenosis are associated with mitral stenosis, it is usually difficult to differentiate the two murmurs. One method is to note the intensity of the diastolic or presystolic murmur as the stethoscope is moved from the apex toward the lower sternum, and then toward the right nipple The murmur should decrease in intensity, and then increase as the right border of the sternum is reached and the right nipple approached

Abnormal Murmurs at the Apex

Abnormal Systolic Murmurs at the Apex.—An abnormal systolic murmur at the apex may occur in three ways:

1 *Organic Mitral Insufficiency*—This occurs with acute and chronic rheumatic heart disease. During the acute stage, tiny verrucae form along the closure lines of the mitral valve and may prevent complete closure, but this is not important. In the later states of mitral disease, the chordae become shortened, and the valve cusps thickened and rigid, all of which interfere with closure of the valve during ventricular systole

2 *Functional Mitral Insufficiency Due to Dilatation of the Heart.*—Dilatation of the heart occurs in hypertensive cardiovascular disease with left ventricular failure, severe anemias, acute rheumatic fever, or acute carditis from any cause, *etc* Dilatation can cause mitral insufficiency in the following ways

a With dilatation, there is weakness of the muscles surrounding the fibrous ring of the mitral valve During systole, the *a–v* valves close not only by means of coaptation of the valve edges but also by means of contraction of the ventricular muscle, transforming the valve into a thin narrow slit The muscular weakness associated with dilatation may be sufficient to prevent complete closure of the valve.

b With dilatation, the papillary muscles and the chordae tendineæ which are attached to the valves are displaced downward. If the chordae do not stretch sufficiently, they prevent complete closure of the valve.

3 Transmission of a Systolic Murmur From the Base.

Differential Diagnosis of Apical Systolic Murmurs.—When the murmur is soft and occupies only a portion of systole, there may be no way of determining from the murmur alone, whether it is normal or abnormal. When the murmur is moderately loud (grade 3 or more), and is heard outside the apex, and transmitted toward the axilla, I believe that it should be considered abnormal However, an abnormal murmur, due to organic or functional mitral insufficiency, may have only the characteristics of a normal murmur In such cases, the presence of physical, fluoroscopic, electrocardiographic and other laboratory signs of cardiac enlargement suggests that the murmur is abnormal Exercising the patient, placing him on the left side, or having him sit and lean forward and to the left will accentuate both normal and abnormal apical systolic murmurs A prolonged murmur occupying most or all of systole and masking the first sound is also evidence of abnormality A harsh, screeching, "sea-gull" murmur, or a musical, or very loud systolic apical murmur is often due to ruptured chordae, unusual valve deformity, or aberrant strands or bands in the ventricular cavity.

Systolic expansion of the left auricle, observed on fluoroscopic examination (page 190) can be used to differentiate the systolic murmur of mitral insufficiency from a normal systolic murmur

The diagnosis of a transmitted apical systolic murmur is made by finding a more intense murmur with the same pitch, timing, and duration at some point higher on the chest. However, in some cases of aortic stenosis only an apical systolic murmur is heard. When this happens, the diagnosis of aortic stenosis may be impossible unless one sees calcification of the aortic valve on fluoroscopic or *x*-ray examination.

Phonocardiographic analysis has been used in an attempt to differentiate normal from abnormal apical systolic murmurs, with questionable results. However, it has been recently pointed out that when the phonocardiogram is taken simultaneously with the electrocardiogram, a normal systolic murmur begins after the *S* wave of the electrocardiogram or after the *QRS* complex, whereas, in mitral disease, the murmur begins within the *QRS* complex Another point of differentiation is that normal murmurs tend to be of one frequency, whereas abnormal apical systolic murmurs tend to be composed of a combination of high and low frequency vibrations (see page 50)

In addition, phonocardiographic analysis of a normal systolic apical murmur shows a relatively silent gap between the first sound which precedes the murmur and the second sound which follows When the systolic murmur is due to organic mitral insufficiency, it usually is present throughout most of systole

The interpretation of an apical systolic murmur in a patient with rheumatic heart disease and mitral stenosis is discussed on page 524

Abnormal Diastolic and Presystolic Murmurs at the Apex.—Abnormal diastolic and presystolic murmurs at the apex can occur in the following ways:

1 *Organic Mitral Stenosis.*—When the mitral valve is involved in chronic rheumatic heart disease, fibrosis and fusion of the cusps may occur, beginning at the commissures This results in a decreased circumference of the valve orifice, which becomes still smaller as the fibrous tissue shrinks, resulting finally in a slit-like opening, the so-called button-hole form of mitral stenosis In other cases, fusion of the cusps with one another and with the chordae tendinedae converts the mitral valve into an irregular small funnel-shaped structure This is the so-called funnel form of mitral stenosis. In either case, the passage of blood into the ventricles during diastole causes the valves to vibrate with resultant murmur formation.

The diastolic murmur of mitral stenosis is usually *soft*, low-pitched, rough and rumbling It never masks the second sound and is separated from it by an audible interval, because the second sound is produced by closure of the semilunar valves, whereas the diastolic murmur does not begin until after the *a-v* valves open The murmur is heard over a comparatively small area near the apex However, the apex in such cases is often near the axilla, and I make a point of carefully auscultating the left axilla in all cases of suspected mitral stenosis. The murmur can sometimes only be heard after exercise and by having the patient lie in the left lateral position. The type of exercise used depends on the patient. Ambulatory patients can be made to hop on one foot 25 times Bed-ridden patients are asked to sit up and lie down 10 times, or until the heart rate increases. The inhalation of amyl nitrite has been also used to increase the heart rate, but I do not use it nor recommend it for this purpose The bell type stethoscope should be used because it is best for low-pitched murmurs.

This diastolic murmur is frequently accompanied by adjuvant auscultatory signs of mitral stenosis, namely a sharp first sound at the apex (page 157), an opening snap of the mitral valve (page 159), and a loud and split pulmonary second sound, with possibly a systolic or a diastolic murmur or both at the pulmonary area (page 163)

Presystolic accentuation of the diastolic murmur occurs when the auricles contract forcibly late in diastole, increasing the flow of blood. This is immediately followed by the sharp first sound which gives the murmur an illusory crescendo accentuation. However, when mitral stenosis is associated with auricular fibrillation, active auricular contractions disappear and the presystolic component of the diastolic murmur also disappears.

2. *Relative or Functional Mitral Stenosis.*—This occurs particularly in cases of cardiac dilatation due to left-sided heart failure, acute rheumatic carditis, acute infectious carditis, severe anemias, especially sickle cell anemia, and aortic insufficiency, especially syphilitic. In such cases, the dilatation of the left auricle and left ventricle in the presence of a vigorously acting heart produce in effect a relative stenosis of the mitral valve and a murmur, caused by the swirling of blood as it passes into the enlarged left ventricle. Rarely, functional mitral stenosis can be caused by a tumor or a large thrombus of the left auricle.

Functional mitral stenosis with an apical diastolic murmur can also occur in congenital heart disease, especially in cases of patent ductus arteriosus, or auricular or ventricular septal defects.

The murmurs of functional mitral stenosis are identical with those of organic mitral stenosis. However, they are transient and disappear when compensation is restored. It is important to be able to recognize that the murmurs may be functional. For example, the occurrence of a diastolic apical murmur during a first attack of acute rheumatic fever should not lead to a mistaken diagnosis of mitral stenosis, because it requires several years of valve scarring to produce organic stenosis. Similarly, during an acute exacerbation of sickle cell anemia, where the clinical picture is in many respects similar to rheumatic fever (see page 724), the presence of diastolic and presystolic murmurs should not lead to the erroneous diagnosis of rheumatic heart disease and mitral stenosis.

When the presystolic apical murmur occurs in a patient with aortic insufficiency, it is called an Austin Flint murmur. Numerous explanations for the Austin Flint murmur have been offered in the past, but the fact that it is not present in well-compensated cases of aortic insufficiency, but only when left ventricular failure is present, disappearing when compensation occurs, suggests that it is produced in much the same way as the apical diastolic and presystolic murmurs of functional mitral stenosis. The reason that the Austin Flint murmur is not heard in ordinary cases of left ventricular failure, but rather a gallop, is in all probability the fact that the blood flow is not rapid enough in such hearts.

Functional mitral stenosis with an apical diastolic murmur, occurring in an auricular septal defect may simulate the Lutembacher syndrome (auricular septal defect plus organic mitral stenosis). However, if the murmur is functional, the first sound is not accentuated and an opening snap of the mitral valve (page 159) will not be present.

In cases where an apical diastolic murmur is suspected, the murmur can often be accentuated by having the patient exercise and then immediately examining him in the right or left lateral decubitus position.

3. *Transmitted Apical Diastolic Murmurs.*—The diastolic murmur of aortic insufficiency, and that of pulmonary insufficiency (the Graham Steell murmur) may be transmitted to the apex.

Differential Diagnosis of Apical Diastolic Murmurs.—When in addition to the murmur, the opening snap of the mitral valve is present, this is pathognomonic of organic mitral stenosis. As a matter of fact, the opening snap alone is pathognomonic of mitral stenosis (page 159). Otherwise, the sharp first sound, the presystolic accentuation of the murmur, the splitting of a loud pulmonary second sound can all occur with functional mitral stenosis. In organic mitral stenosis, characteristic enlargement of the left auricle is present, whereas there is generalized cardiac dilatation in sickle cell anemia, acute rheumatic carditis, *etc.* When aortic insufficiency is the cause of the apical diastolic murmur, other characteristic auscultatory and peripheral signs of the aortic insufficiency are present. However, in aortic insufficiency it may be impossible to determine if organic mitral stenosis is also present, unless marked enlargement of the left auricle is also found The accentuated and sometimes slurred first heart sound of a rapidly beating heart in a thin person should not be confused with mitral stenosis. Differentiation of transmitted aortic and pulmonic diastolic murmurs from the murmur of mitral stenosis (relative or organic) is simple, because aortic and pulmonic diastolic transmitted murmurs are soft and blowing, not rumbling, they have a diminuendo quality, there is never any presystolic accentuation, and the aortic and pulmonary diastolic murmurs immediately follow the second sound, whereas with the mitral diastolic murmur, the murmur follows the second sound after an audible interval.

Precordial Noises Heard at a Distance from the Chest.—The most common causes of such loud sounds or noises are cardiac murmurs due to rupture of a valve, or interstitial mediastinal or pulmonary emphysema, or spontaneous or traumatic pneumothorax, pneumopericardium, noises the heart produces by striking air-containing gut, or air embolism

Abnormal Physical Signs in the Lungs

Pleural Effusion (*Hydrothorax*).—Small effusions of less than 400 or 500 cc are difficult to diagnose by physical examination When the effusion exceeds this amount, typical findings include.

1. A decreased inspiratory expansion of the affected side of the chest This, of course, is not pathognomonic of pleural effusion.

2 Flatness on percussion, corresponding roughly to the level of the fluid In addition, the skin imparts a sense of resistance to the percussing finger In moderate effusions, the flatness is first noted posteriorly over the lung bases. Normally the lowest level of pulmonary resonance is at the level of the ninth or tenth thoracic vertebra With fluid, the flatness ascends, and approaches and may rise above the angle of the scapula (which lies at the level of the seventh thoracic vertebra). Above the flat zone, there may be a zone of tympany, due to the fact that the fluid pushes up and relaxes the lung tissue The flat percussion note also extends anteriorly and may merge with the flatness of the heart on the right or left side In addition, the heart can be displaced by the effusion. This is especially so with large left pleural effusions which can displace the heart to the right so that the apex appears near the sternal border. In addition, a right pleural effusion can displace the liver below the costal margin

A characteristic finding of the area of flatness of a pleural effusion, anteriorly or posteriorly, is that if the upper levels of flatness are marked with a skin crayon or ink, an irregular S-shaped line results, because the fluid rises to different levels in different regions of the chest

3. Over the area of flatness, tactile fremitus is usually absent or very faint, and the breath sounds are usually feeble or absent. Occasionally, bronchial breath sounds may appear, due to compression of the lung tissue by the fluid

Clinical Significance of Pleural Effusion.—Pleural effusion can occur in the following conditions.

1. *Heart Failure*—Pleural effusion can be considered a localized form of edema, as was pointed out on page 127 However, subcutaneous edema and pleural effusion may occur together or independently of each other. Since both the pulmonary veins and the superior vena cava, by way of the azygos vein, drain the pleura, left-sided heart failure with an increased venous pressure in the pulmonary veins can occur without pleural effusion, and right-sided heart failure, with an increased pressure in the superior vena cava, can occur without pleural effusion. Therefore, when effusion occurs as a result of heart failure, one can assume that both right- and left-sided heart failure are present

Isolated right pleural effusion is much more common than isolated left pleural effusion after heart failure, and when bilateral effusion is present, much more fluid is usually present on the right side than on the left. The cause of this is obscure. One explanation is based on the anatomical nature of the venous return of the blood from the pleural cavities. On the right side, drainage is by way of the major azygos vein directly into the superior vena cava When the pressure in the superior vena cava increases, the pressure in the azygos vein is directly affected, and right pleural effusion develops The left pleural cavity is largely drained by way of the minor azygos vein, which usually empties into the left innominate vein, so that even when the the pressure in the superior vena cava is high, it does not directly affect the pressure in the minor azygos vein.

It has also been noted that in the lying position, blood from the right lung must run uphill about 10 cm. through the right pulmonary veins against a force of gravity to reach the left auricle, whereas blood in the left lung has to flow uphill only 5 cm Therefore right pleural effusion is more common than left. More study of this interesting problem is needed.

Isolated left pleural effusion as a result of heart failure is uncommon as was just mentioned. Occasionally it occurs, especially when the right pleural cavity is obliterated by fibrous adhesions Rarely the effusion is localized to an interlobar fissure.

The fluid is usually clear, straw-colored, occasionally amber, and shows the characteristics of a transudate, namely a specific gravity below 1 018 Occasionally there are many white and red blood cells present and large plaques of pleural endothelial cells.

2 *Pulmonary Infarction.*—Pulmonary infarction does not result in pleural effusion as often as heart failure does. The fluid may be identical with that of failure. Occasionally it is grossly bloody; and isolated left pleural effusion after pulmonary infarction is comparatively common.

3. *Rheumatic Pleuritis and Effusion* —This is a comparatively uncommon cause of pleural effusion. It occurs during the course of acute rheumatic fever, and it may be very difficult to determine whether the effusion is due to an inflammatory pleuritis or to heart failure. The pleural effusion which occurs during the course of disseminated lupus erythematosus can be considered in a similar category

4. *Noncardiac Causes of Pleural Effusion.*—The most common of these is tuberculous pleurisy with effusion. Malignancy of the lungs and pleura can also cause effusion. Rarely effusion occurs with cirrhosis of the liver, with benign ovarian neoplasms (Meigs's syndrome), nephritis, *etc*

Abnormal Breath Sounds.—When left-sided heart failure occurs, moist rales appear at the bases of both lung fields, and as the pulmonary edema becomes aggravated, the rales spread throughout the lungs, posteriorly and anteriorly However, the physician who waits for the appearance of these rales before diagnosing left heart failure will overlook many early cases of failure, where the lungs sound normal in spite of pulmonary congestion.

Rarely, during an attack of acute pulmonary edema, an expiratory type of dyspnea with sibilant and sonorous rales may occur which can completely simulate an attack of bronchial asthma (cardiac asthma). However, in such cases, other signs of cardiac pathology, such as enlargement of the heart, a paroxysmal rise in blood pressure, abnormal circulation time values, *etc.*, are present.

Localized moist rales occasionally occur after pulmonary embolism and infarction, but the findings are not characteristic of pulmonary infarction The presence of bronchial breath sounds over a pleural effusion has already been mentioned. The appearance of rales with many forms of pulmonary pathology need not be discussed here.

Ewart's Sign.—In 1896, Ewart described the appearance of an area of dullness on percussion, increased fremitus and bronchial breathing at the angle of the left scapula, as a sign of pericardial effusion. He ascribed it to compression of the left lung by the pericardial effusion However, the sign is inconstant, and may be absent even with large pericardial effusions, and many cardiologists have questioned Ewart's explanation. For example, the sign may merely be an indication of an associated pneumonitis.

Abnormal Physical Signs in the Abdomen

Enlargement of the Liver.—Enlargement of the liver may occur in the following conditions:

1. *Right-Sided Heart Failure* —Enlargement of the liver may occur very early, even within a few minutes after right-sided heart failure develops It is generally believed that the enlargement is due to passive congestion as a result of the increased pressure in the inferior vena cava, transmitted to the hepatic veins However, there is some evidence that the enlargement and engorgement of the liver is an active compensatory mechanism initiated by reflexes in the distended right auricle and vena cavæ, to prevent overloading of the heart, rather than as the simple effect of increased venous pressure One point in favor of this theory is that in cases of moderate right-

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The factors which cause ascites of cardiac origin can be described in the following way:

1. The first factor responsible for ascites is a retention of salt and water, just as occurs in the formation of edema (see page 127).

2. The second factor is an increased pressure in the inferior vena cava and in the hepatic veins and their tributaries, namely, the central veins and the hepatic sinusoids. The increased pressure in the central veins and the sinusoids causes a transudation of fluid into the interstitial tissue of the liver This fluid then passes into the free peritoneal cavity directly across the liver capsule by way of the thin-walled lymphatics which lie beneath the capsule.

It is not necessary to have an increased pressure in the portal vein for ascites to occur. It has been shown experimentally that if the portal vein, or the inferior vena cava, below the insertion of the hepatic veins, is ligated, ascites will not develop. However, if the inferior vena cava in the thorax, or the hepatic veins are ligated, liver congestion occurs, salt and water are retained, and ascites develops.

3. Hypoalbuminemia.—The presence of hypoalbuminemia, which reduces the osmotic pressure of the serum, is another factor which aids in the formation of ascites.

4. Hormonal factors.—Hepatic congestion can cause increased activity of the antidiuretic hormone of the posterior pituitary In addition, there is some evidence that congestion of the liver is accompanied by an increased production of adrenal cortical steroids similar to the mineralocorticoid desoxycorticosterone, which induces the retention of salt and water.

The term *cardiac cirrhosis* has been used to designate cases of ascites and splenomegaly due to chronic right-sided heart failure (usually due to mitral stenosis with or without tricuspid stenosis). In such cases, the liver presents a characteristic appearance. It is markedly engorged In the center of each lobule the central vein is markedly distended The surrounding cells show atrophy and even focal hemorrhagic necrosis Hyperplasia of the connective tissue framework of the liver may occur with scattered regeneration of the liver cells

Ascites due to heart failure is sometimes mistakenly diagnosed as cirrhosis of the liver, especially since pleural effusion can also occur with cirrhosis. However, in cirrhosis, the venous pressure in the upper extremities is normal, and a normal hepato-jugular reflux (page 110) is present Furthermore, signs of marked cardiac enlargement are absent

Diagnosis of Ascites.—In addition to the protruberant abdomen, a very characteristic protrusion of the umbilicus occurs Abnormal percussion signs are also present since the fluid gravitates to the flanks, floating the intestines up Therefore, with the patient lying, dullness is present in the flanks and resonance in the umbilical region. However, when the patient turns on his side, the uppermost flank becomes resonant and the umbilical region dull. I have found these signs of greater value than the "fluctuation wave" felt by the hand on one flank while the other flank is sharply tapped The fluctuation wave can be brought out more clearly by having the patient sit up

sided heart failure, the liver may be enlarged when the venous pressure is normal.

Downward displacement of the liver by a right pleural effusion or by a large pericardial effusion should not be mistaken for enlargement of the liver.

2. *Constrictive Pericarditis*.—The mechanism for enlargement is similar to that which occurs in right heart failure. (Also see page 650.)

3. *Noncardiac Conditions*.—The most common of these is cirrhosis of the liver. The other noncardiac causes of hepatomegaly need not be discussed here.

Pulsations of the Liver.—Two types of true liver pulsation may occur:

1. *Ventricular or Systolic Pulsation of the Liver*.—This can be diagnosed in the following way. Place one hand over the liver anteriorly and the other posteriorly over the liver. Both hands can be felt to be separated by the expansile pulsation of the liver, which is synchronous with ventricular contraction.

Systolic pulsation of the liver occurs with tricuspid insufficiency, which is usually functional and due to acute right-sided heart failure. Because of the tricuspid insufficiency, the blood expelled from the right ventricle regurgitates into the right auricle and into the inferior vena cava and liver. Blood also regurgitates into the superior vena cava and the jugular veins, so that marked systolic pulsations of the jugular veins may also appear. It is possible that a systolic-like pulsation of the liver can occur without tricuspid insufficiency, merely being due to engorgement and stagnation of blood during systole with a transient decrease in engorgement during diastole, just as the ventricular form of the venous pulse is formed (page 149). A systolic liver pulsation may also occur in nodal rhythm.

2. *Auricular or Presystolic Pulsation of the Liver*.—In cases of severe right-sided heart failure, contraction of a large, forceful right auricle can propel sufficient blood into the inferior vena cava and liver to cause a palpable presystolic pulsation. This usually occurs when tricuspid stenosis hinders the flow of blood into the right ventricle, but a presystolic liver pulsation is not pathognomonic of it. A presystolic liver pulsation is very difficult to diagnose by physical examination, and should be confirmed by pulse tracings of the liver.

Transmitted Liver Pulsations.—Pulsation of a hypertrophied right ventricle or of the abdominal aorta can be transmitted to the liver. These are localized unlike the diffuse systolic or presystolic pulsation described above.

Other Abnormal Abdominal Pulsations.—Although marked pulsations of the aorta are commonly felt in normal people, especially if they are thin, an expansile pulsation in the abdomen is abnormal and may be due to aneurism of the abdominal aorta or of one of the visceral arteries. A systolic bruit can be heard over the abdomen in such cases. In rare cases of aortic or tricuspid insufficiency, pulsation of the spleen may occur. The transmission of the pulsation of a normal aorta through a cystic abdominal tumor should not be mistaken for an aneurism.

Ascites.—The most common condition in which ascites appears is cirrhosis of the liver. However, it is a part of the syndrome of constrictive pericarditis and can occur in cases of severe, chronic, right-sided heart failure.

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Enlargement of the Spleen.—The method of palpating the spleen is described on page 46 The spleen should not be palpable normally. A palpable spleen can occur in the following conditions.

1 *Acute and Subacute Bacterial Endocarditis.*—Moderate enlargement usually occurs, though sometimes the spleen may be massive The enlargement is due to the infective process, sometimes to emboli and splenic infarcts Rarely the spleen becomes palpable during acute rheumatic fever.

2. *Chronic Right-sided Heart Failure*—In chronic right-sided heart failure, the spleen is usually small However, it may become enlarged merely as a result of chronic congestion A large spleen may also occur in constrictive pericarditis

3 *Noncardiac Conditions*—These will not be discussed here

Dilated Superficial Abdominal Veins.—Dilated and tortuous superficial veins may appear over the upper part of the body and upper abdomen in obstruction of the superior vena cava, and over the lower abdomen and lower extremities in obstruction of the inferior vena cava These veins show a reversed flow of blood The method of eliciting this is described on page 559

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Chapter 9

ABNORMAL FINDINGS ON FLUOROSCOPIC AND X-RAY EXAMINATION

ENLARGEMENT OF THE LEFT VENTRICLE (Figs 39, 40)

THE left ventricle can be divided into an inflow tract and an outflow tract. The inflow tract lies between the mitral valve and the apex of the left ventricle and includes the posterior half of the interventricular septum and the posterolateral wall of the left ventricle. The outflow tract lies between the apex and the aortic valve and includes the anterior half of the interventricular septum and the anterolateral wall the left ventricle Thus in the *P-A* position, the border of the outflow tract appears, whereas in the L.A O. position, the inflow tract can be seen. It has been suggested that the outflow tract first enlarges and later the inflow tract.

P-A Position —Enlargement of the left ventricle in the *P-A* position is indicated by. (1) an increased rounding of its left border; (2) extension of the left ventricular shadow below the diaphragm where it will be seen within the gas bubble of the stomach or colon. Normally, the left ventricular segment ends above the dome of the diaphragm.

A normal horizontal heart may simulate left ventricular enlargement, especially if a large apical fat pad is present Differentiation is possible by having the patient take a deep breath. This causes the rounding of a normal horizontal heart to disappear

R.A.O. Position.—The signs of left ventricular enlargement are minimal in this position The esophagus is usually not displaced, but when the enlargement is marked, posterior displacement of the esophagus may occur due to concomitant enlargement of the left auricle. Similarly, if the aorta is tortuous and dilated, in association with the large left ventricle, it may pull the esophagus, which is attached to it by fibrous adhesions, posteriorly and to the left

L A.O. Position.—The posterior contour of the left ventricle becomes rounder than normal and bulges posteriorly, so that it reaches and may overlap the shadow of the spine. The so-called interventricular groove is displaced downward below the diaphragm It has been suggested that inability of the left ventricle to clear the spine when the patient is turned at an angle of 55° is a sign of left ventricular enlargement. However, actual measurement of the angle at which the patient is standing is impractical.

Differentiation of Left Ventricular Hypertrophy From Dilatation of the Heart.—Hypertrophy is usually present with some degree of dilatation, but from fluoroscopic or *x*-ray examination, it is not possible to differentiate enlargement caused by hypertrophy or dilatation, although it has been stated that pure hypertrophy results in a change in the shape of the heart, whereas dilatation leads to general enlargement. For this reason, the term

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Abnormal Abdominal Pulsations

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Ventricular Aneurism (Fig. 43) —This usually occurs as a result of a previous myocardial infarction. A localized bulge of a portion of the ventricular wall occurs. On fluoroscopy, such a bulge may show a paradoxical systolic expansion in contrast to the systolic contraction of the normal surrounding muscle. Occasionally only diminished pulsations occur locally, but this is not characteristic of aneurism and can occur when the heart is merely enlarged On occasion, calcification of the thin aneurismal wall occurs. Roentgenkymographic or electrokymographic examination will also show abnormal systolic expansile pulsations over the aneurism.

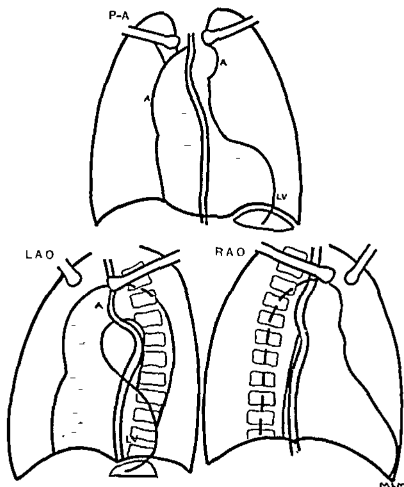


FIG 41 —Marked enlargement of the left ventricle In addition, there is generalized dilatation and tortuosity of the aorta

enlargement is used. However, under certain conditions, such as marked anemia, diphtheria, acute rheumatic carditis, acute heart failure, acute glomerular nephritis, *etc*, acute dilatation of the heart may occur. This is characterized by a rapid, generalized increase of the cardiac shadow, in association with signs of pulmonary congestion or edema. Similarly, generalized dilatation may appear in the later stages of severe chronic heart failure, or with infectious myocarditis, beriberi, peripheral *a–v* fistulas, *etc*, Figure 42, *A* shows acute dilatation of the heart which occurred in a patient with chronic rheumatic heart disease. Figure 42, *B* shows the heart three months later, when compensation had been restored. Notice that when dilatation of the heart was present, the outline of the heart was indistinct, and differentiation of the individual chambers extremely difficult.

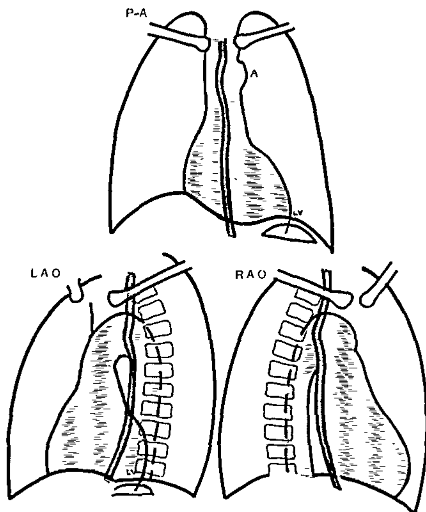


Fig. 40 —Moderate enlargement of the left ventricle.

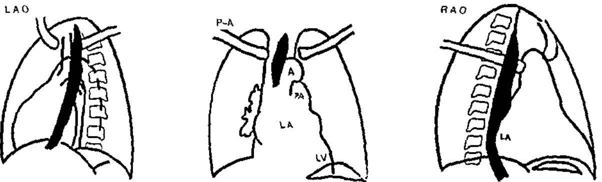


FIG 42 —*B*, Same patient three months later The size of the heart has decreased greatly and the outline of the individual cardiac chambers is now visible Enlargement of the right ventricle, left auricle, and dilatation of the pulmonary artery are present The patient had rheumatic heart disease with mitral stenosis

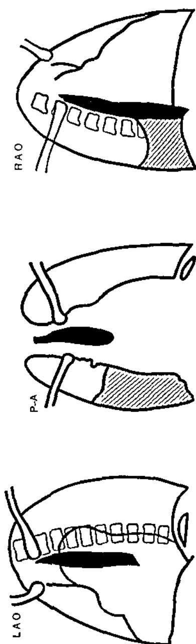


Fig 42 —A, Generalized dilatation of the heart due to heart failure Notice the right pleural effusion in the P-A and R A O. positions.

that even though the cardiac contour appears normal in the conventional *P–A* position, the interventricular septum, which normally is convex to the right, becomes convex to the left because of the right ventricular hypertrophy.

The increase in the transverse diameter of the heart to the left is not characteristic of right ventricular enlargement, and can also occur with left ventricular enlargement. In the later stage of right ventricular enlargement, there may be associated enlargement of the cardiac shadow to the right, due to enlargement of the right auricle, left auricle, or both. When marked right ventricular enlargement is present in congenital lesions, such as pulmonary stenosis, the tetralogy of Fallot, the Eisenmenger complex, *etc*, the apex of the heart is characteristically elevated and blunt, and lifted above the diaphragm, giving a boot-like appearance (Fig. 90, page 419).

Right ventricular enlargement is often associated with dilatation or displacement of the pulmonary artery, so that in the *P–A* position, a prominent pulmonary artery segment appears on the left border of the heart. Dilatation of the pulmonary artery may be the result of increased pressure within the pulmonary circuit as in cases of chronic pulmonary disease, patent ductus arteriosus, the Eisenmenger complex, interauricular septal defects, *etc.*, or the result of post-stenotic dilatation of the pulmonary artery, such as occurs with congenital pulmonary stenosis

Displacement of the pulmonary artery occurs particularly in cases of mitral stenosis Here the enlarged right ventricle pushes the pulmonary artery upward, while the large left auricle, which is usually present, pushes the pulmonary artery and the right ventricle anteriorly. The straightening of the left middle border of the heart in the *P–A* position, in cases of mitral stenosis, is not due to prominence of the pulmonary conus as some observers have thought, but is due to both the prominent pulmonary artery and its left main branch, and to the extension of the large left auricle or the left auricular appendage along the left border of the heart (Figs. 42, *B*, 45).

R A O. Position.—The enlarged right ventricle bulges into the retrosternal space, tending to obliterate it (Fig. 45). Enlargement of the pulmonary artery segment may or may not be present.

L A O Position—The enlarged right ventricle causes a bulge in the lower portion of its contour anteriorly At the upper end of this bulge, an angulation may be present, This marks the junction of the right ventricle with an enlarged right auricular appendage (Fig. 45) The right ventricular contour can be traced diaphragmatically, and occasionally the interventricular groove is seen to be displaced posteriorly.

ENLARGEMENT OF THE LEFT AURICLE (Figs 42, *B*, 44, 45)

P–A Position—An enlarged left auricle extends both to the left and right. On the left side of the heart, the enlargement causes straightening and outward bowing of the left border of the heart below the pulmonary artery This has been proven by angiocardiographic studies In addition, enlargement to the right may be sufficient to bring the left auricular shadow to the

ENLARGEMENT OF THE RIGHT VENTRICLE (Figs. 44, 45)

An inflow and an outflow tract have also been described for the right ventricle The inflow tract extends from the tricuspid valve to the apex of the right ventricle The outflow tract extends from the apex of the right ventricle to the pulmonary valve. Enlargement of the inflow tract takes place chiefly along the diaphragmatic surface of the right ventricle, and can be best observed in the L A.O. position. The outflow tract is seen well in the R A O position.

P-A Position.—The cardiac silhouette may remain normal in the *P–A* position even when considerable enlargement of the right ventricle is present, unless serial *x*-rays are taken In such cases, widening of the transverse diameter of the heart appears Angiocardiographic studies indicate

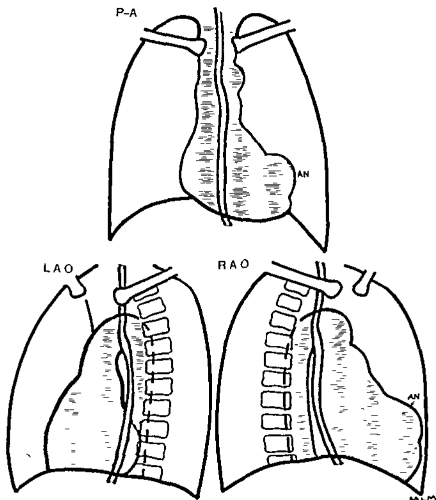


FIG. 43 —Ventricular aneurism. AN, The aneurism.

L.A.O. Position.—Marked enlargement of the left auricle lifts the lef main bronchus upward, and may compress it (Fig. 45). Although elevation of the bronchus can occur with left auricular enlargement from any cause compression is almost invariably due to rheumatic heart disease, because the compression must have occurred during childhood when the chondral rings were still pliable

Left Lateral Position.—Enlargement of the left auricle can sometimes be seen better in the *left lateral* position than in the *R.A.O.*, or *L.A.O.* position. In the *left lateral* position, an enlarged left auricle presses on the middle third of the barium-filled esophagus, and causes obvious narrowing and posterior displacement of the esophageal shadow.

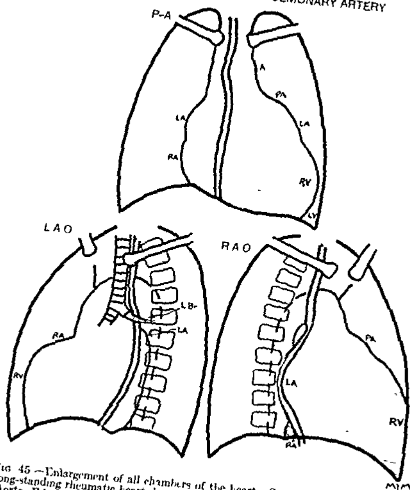


Fig. 45.—Enlargement of all chambers of the heart. Such a silhouette would occur long-standing rheumatic heart disease with marked involvement of the mitral valve. Aorta, RA, right auricle. Also see caption of figure 44.

right border of the heart where it can be visualized above and within the right auricular shadow, forming a double density (Fig. 42 *B*). The esophagus is usually displaced by the large left auricle to the right in the *P–A* position Occasionally the large left auricle displaces it to the left.

R.A.O. Position —This is the best position for observing left auricular enlargement. The enlarged left auricle sharply compresses and then displaces the barium-filled esophagus, and tends to obliterate the retrocardiac space (Figs 42, *B*, 44, 45). Normally, a slight posterior bowing of the esophagus may occur This should not be confused with the localized posterior displacement caused by a large left auricle. The normal bowing tends to disappear on deep inspiration

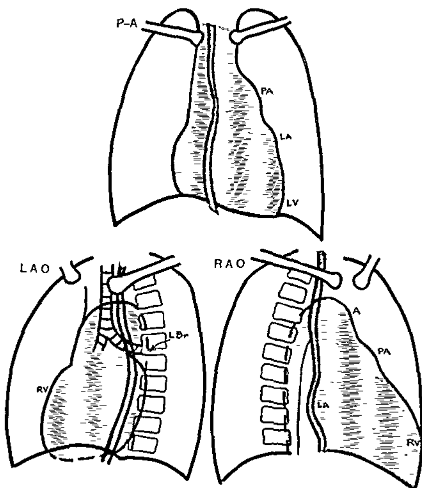


Fig 44 —Enlargement of the right ventricle, RV; left auricle, LA; and dilatation of the pulmonary artery, PA This configuration is typical of rheumatic heart disease with mitral stenosis, LBr, left bronchus

SYSTOLIC EXPANSION OF THE LEFT AURICLE

Recent advances in the surgery of mitral stenosis have made it important to determine whether any significant mitral insufficiency is present. One way in which this can be done is to find a systolic expansile pulsation of the left auricle in either the *P-A* or *R.A.O* position

P-A Position (Fig 46).—When a large left auricle extends to the right border of the heart and forms a double contour with the right auricle, the left auricle will move outward (toward the right) and the right auricle will move inward (toward the left) during systole, producing a seesaw movement The outward movement of the left auricle is due to the regurgitation

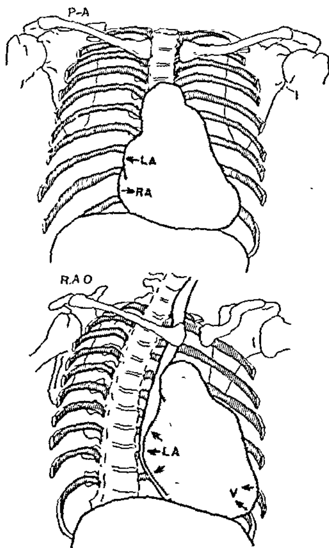


Fig. 46.—Fluoroscopic diagnosis of systolic expansion of the left auricle (after Elkin, Sosman, Harken, and Dexter).

of blood from the left ventricle during systole The inward movement of the right auricle is due to the transmitted contraction of the right ventricle This sign is not always present in mitral insufficiency. If tricuspid insufficiency is also present with the mitral insufficiency, both the right and left auricles will move outward during systole

R.A.O. Position (Fig 46).—The left auricle moves posteriorly during systole, whereas, the right ventricle moves inward.

Posterior expansion of the left auricle in the *R.A O.* position can also occur when mitral insufficiency is not present For example, a large right ventricle may push the left auricle backward during systole, even if mitral insufficiency is absent If tricuspid insufficiency is present, the expansile right auricle also may push the left auricle posteriorly even if mitral insufficiency is absent Conversely, the left auricle may not show posterior systolic expansion even if mitral insufficiency is present This may be caused by a thickened, rigid, left auricular wall

ENLARGEMENT OF THE RIGHT AURICLE

P-A Position.—Normally the trabeculated portion of the right auricular appendage forms the right lower border of the heart in the *P-A* position Enlargement of the right auricle causes the right auricular shadow to extend further to the right.

R.A.O. Position —The left auricle overlies most of the right auricle in this position except near the diaphragm, so that when marked right auricular enlargement is present, it fills the retrocardiac space immediately below the diaphragm and behind the esophagus (Fig. 45) However, part of this shadow may be due to a dilated inferior vena cava

L.A.O. Position.—Enlargement of the right auricle causes a horizontal shelf to appear between the right ventricle and the aorta (Fig 45)

ABNORMALITIES OF THE AORTA

Dilatation, Tortuosity and Elongation of the Aorta.—P-A Position. As the dilated aorta ascends from the heart, it frequently curves to the right, widening the transverse diameter of the base of the heart (Fig 41 page 183) The transverse portion of the arch reaches or extends above the level of the clavicles, and the aortic knob is prominent, extending into the left lung field A rim of calcium is frequently seen within the shadow of the knob The trachea may be displaced to the right The esophagus is frequently displaced to the left, just below the indentation of the aortic knob This is due to the fact that as the aorta swings over to the left, it pulls the esophagus, which is connected to it by fibrous bands.

R.A.O. Position.—The shadows of the ascending and descending aorta are not well visualized in this position. The posterior displacement of the aorta draws the esophagus posteriorly, away from the left auricle, so that the esophagus cannot be used to determine left auricular enlargement when dilatation and tortuosity of the aorta are present.

L.A.O. Position.—The aorta swings up from the shadow of the heart with anterior bowing instead of rising vertically The aortic arch is broad, and the anterior and descending limbs are clearly visible and widely separated, the descending limb being displaced posteriorly behind the spine. Backward displacement of the esophagus occurs just below the aortic knob (Fig. 41, page 183)

Widened brachiocephalic vessels may appear with dilatation of the aorta Thus, dilatation of the innominate or right subclavian artery is seen as an oblique shadow running upward and to the right, at the base of the heart on the right side in the *P–A* position. It should be differentiated from a dilated superior vena cava which runs vertically upward, with or without a convexity to the right A dilated left subclavian artery or left common carotid artery is visible as a rounded projection above the aortic

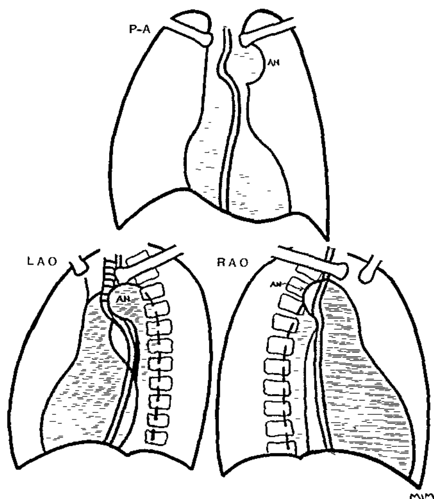


Fig. 47.—Aneurism of the arch of the aorta. AN, The aneurism

knob on the left side in the P-A and R A O positions. This frequently appears with coarctation of the aorta (Fig 101, A page 457)

Aneurism of the Aorta (Fig. 47).—An aortic aneurism is recognized by a localized, dense, smooth, saccular dilatation, which is contiguous with the aorta when viewed in all positions. Pulsations may or may not be present, depending on the presence of thrombi within the aneurism. Occasionally, calcification of the aneurismal wall is present. Single or multiple aneurisms may be present. The heart is not enlarged unless other causes for cardiac enlargement (such as aortic insufficiency, hypertension, *etc.*) are present. The marked aortic widening seen in dynamic dilatation of the aorta should not be misdiagnosed as a fusiform aneurism.

The aneurism may occur on the ascending limb, transverse portion of the arch or the descending limb. Rarely an aneurism of one of the sinuses of Valsalva, at the root of the aorta occurs. An anterior mediastinal mass can be confused with an aortic aneurism, especially if the mass is round and shows transmitted pulsations from the aorta. In such cases, angiocardiography may be necessary for correct diagnosis.

Dissecting Aneurism.—See page 661

ABNORMALITIES OF THE PULMONARY ARTERY AND THE HILAR VESSELS

Abnormal Dilatation of the Pulmonary Artery.—P-A Position.—Dilatation of the trunk and the left main branch of the pulmonary artery is observed as a bulging of the pulmonary artery segment on the left side, and dilatation of the comma-shaped hilar vessels bilaterally (Fig. 48) On fluoroscopy, marked pulsations of the hilar vessels occur. This is particularly marked in cases of interauricular septal defects where the expansile systolic pulsation of the hilar vessels is immediately followed by a sharp diastolic collapse, the so-called hilar dance Calcification of a dilated pulmonary artery rarely occurs

Post-stenotic dilatation of the pulmonary artery and a prominent pulmonary artery segment occur in cases of congenital pulmonic stenosis However, here, the hilar vessels are not prominent, do not pulsate vigorously, and the lung fields are abnormally clear, indicating that little blood is coursing through the lungs because of the pulmonary stenosis

R.A.O. Position.—The pulmonary artery segment is markedly accentuated In addition, if the left pulmonary artery is greatly dilated, it can be seen as a dense circular mass, within the cardiac shadow (Fig 87, page 406) The dilated right branch of the pulmonary artery runs backward and horizontally toward the spine

L A O Position.—A large left pulmonary artery runs backward and horizontally toward the spine and across the left bronchus, obscuring the aortic window A dilated right branch can sometimes be seen as a round dense mass within the cardiac shadow

Absent Pulmonary Artery Segment.—The significance of an absent pulmonary artery segment and decreased hilar markings is discussed on page 418

Aneurism of the Pulmonary Artery.—An aneurism of the stem or one of the major branches of the pulmonary artery can be diagnosed by the presence of a massive, saccular bulge, which is confluent with the pulmonary artery shadow in all positions. The hilar vessels do not pulsate markedly.

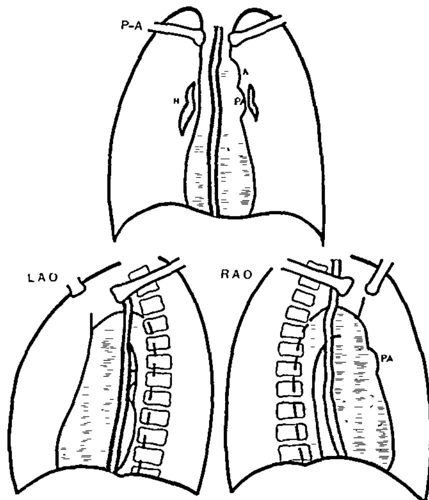


Fig 48 —Moderate dilatation of the pulmonary artery Such a silhouette often occurs in patients with chronic pulmonary disease A, Aorta, PA, pulmonary artery H, Dilated hilar vessels.

ABNORMAL FINDINGS IN THE LUNGS

From a cardiological viewpoint, the important pulmonary abnormalities are pulmonary congestion and edema, pleural effusion, and pulmonary infarction.

Pulmonary Congestion and Edema.—When pulmonary congestion is present, the hilar markings bilaterally are increased in size and density.

This is due to dilatation of both the hilar arteries and veins. There may be diffuse haziness and a fine, marbelized pattern of the lung fields if edema is also present.

In cases of acute pulmonary edema, the haziness of the lung fields may extended fan-like from the hilar regions toward the periphery, leaving the apices, the lateral portions and the bases of the lungs more or less clear (Fig. 49).

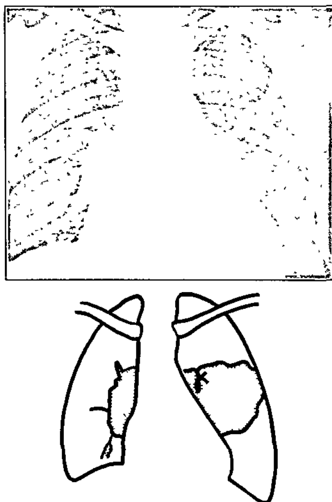


FIG 49 —Acute pulmonary edema.

This picture has been described as characteristic of pulmonary edema occurring during the course of glomerular nephritis, but it can occur with acute pulmonary edema of pure cardiac origin also

In cases of mitral stenosis, with chronic left-sided heart failure, miliary nodules, which may even be calcified, may be scattered throughout the lung fields.

Aneurism of the Pulmonary Artery.—An aneurism of the stem or one of the major branches of the pulmonary artery can be diagnosed by the presence of a massive, saccular bulge, which is confluent with the pulmonary artery shadow in all positions. The hilar vessels do not pulsate markedly.

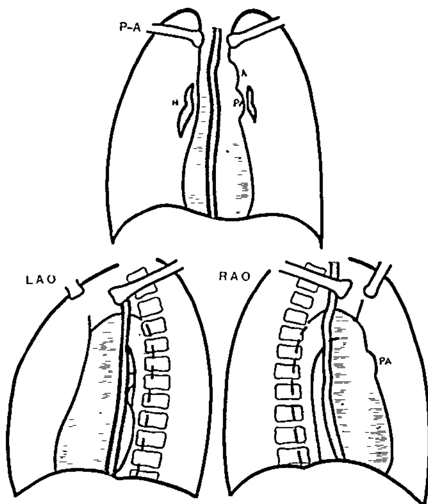


Fig 48.—Moderate dilatation of the pulmonary artery Such a silhouette often occurs in patients with chronic pulmonary disease. A, Aorta, PA, pulmonary artery H, Dilated hilar vessels

ABNORMAL FINDINGS IN THE LUNGS

From a cardiological viewpoint, the important pulmonary abnormalities are pulmonary congestion and edema, pleural effusion, and pulmonary infarction

Pulmonary Congestion and Edema.—When pulmonary congestion is present, the hilar markings bilaterally are increased in size and density.

position is higher and more centrally located than the mitral valve. The locations of the valves in relation to the chest wall are shown in figure 2, page 42. Calcification of the mitral or aortic annulus fibrosus may also occur This appears as a semi-elliptical band of calcification, which also moves with systole.

Other Calcium Deposits.—These may occur within the myocardium or the coronary arteries Myocardial calcification occurs after infarction, especially in the thin wall of a ventricular aneurism. Calcification of the interventricular septum may also occur. Calcification of one of the coronary arteries is recognized by finding smooth, slightly curved, parallel linear deposits. Their superficial location can also be determined by rotating the patient sufficiently. Occasionally, calcification of auricular thrombi may occur.

Calcification of the myocardium can also occur as a result of myocarditis or of excessive administration of vitamin D

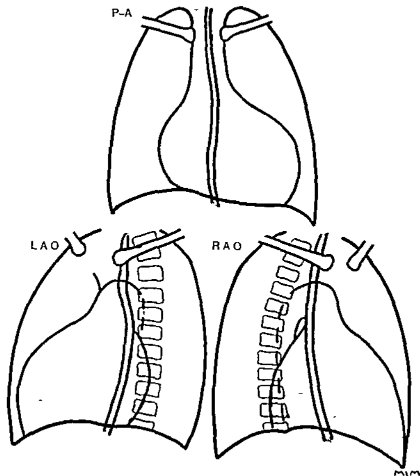


FIG. 50 —Marked pericardial effusion

Pleural Effusion (Fig. 42, *A*).—As has been noted on page 170, pleural effusion due to cardiac decompensation is more common and more marked on the right side. Early signs include the obliteration of the costophrenic sinuses. This can be sometimes better seen in the R.A.O. and L.A.O. positions than in the *P–A* position, because the costophrenic sinuses are deeper posteriorly. Occasionally, the pleural effusion is localized to one or more of the interlobar fissures, rather than occupying the free pleural space. Such localized collections of fluid may resemble tumors, but on rotating the patient sufficiently, the localization of the area of increased density in the region of a fissure can be determined.

Pleural thickening may also occur with long-standing effusion. This produces longitudinal linear streaks just within the ribs, or plate-like areas of increased density, depending on the angle at which the thickened pleura is observed.

Pulmonary Embolism and Infarction.—See page 622.

ABNORMALITIES OF THE PERICARDIUM

Pericardial Effusion.—Effusions of less than 300 cc. are usually not visible. When the effusion exceeds this amount, the cardiac shadow enlarges generally to the right and left. The superior vena cava becomes prominent, and the cardiohepatic angle becomes more acute (Fig. 50). (This should not be confused with Rotch's sign (page 157) on physical examination.) Fluoroscopic examination may show diminished pulsations but this does not always occur. With massive pericardial effusion, the heart has a characteristic bottle-shape, with loss of the normal contours. However, in many cases, the diagnosis of pericardial effusion can only be made from serial *x*-rays which show progressive enlargement of the heart and widening of the transverse diameter, in the absence of pulmonary congestion; and differentiation of pericardial effusion from marked enlargement of the heart may be very difficult. One maneuver that may be of value is to take *x*-ray films in the lying and standing positions, keeping the tube at the same distance from the patient. If pericardial effusion is present, the base of the heart will widen greatly in the lying position.

Constrictive Pericarditis.—See page 652.

PERICARDIAL AND INTRACARDIAC CALCIFICATIONS

Pericardial Calcifications.—These can be recognized as flat, irregular plaques within or at the edge of the heart shadow. The patient should be rotated until the plaque is seen on profile, close to the heart border, indicating its superficial location. These calcified plaques hardly move with systole, but they may move with the heart shadow on inspiration. The deposits may be localized or extensive. They commonly appear on the diaphragmatic surface of the pericardium.

Valvular Calcifications.—Calcification of the mitral or aortic valve, or both, may be present. The calcified valves are seen as irregular, dark, dancing shadows, which may move vertically, obliquely or even in an elliptical course with systole. The aortic valve is closer to the base of the heart than the mitral valve in the *P–A* and R.A.O. positions, and in the L.A.O.

pulmonary artery, dissecting aneurism of the aorta (page 661), obstruction of the superior vena cava, anomalous pulmonary veins draining into the right heart, dextrocardia, transposition of the great vessels, right aortic arch, *etc.*

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CONGENITAL ABNORMALITIES OF THE HEART AND GREAT VESSELS

Dextrocardia.—See pages 398 and 400
Interauricular Septal Defects.—See page 406.
Interventricular Septal Defects.—See page 411.
Eisenmenger Complex.—See page 413.
Tetralogy of Fallot.—See page 418.
Dextroposition of the Aorta.—See page 415.
Congenital Pulmonary Stenosis.—See page 426.
Tricuspid Atresia.—See page 431.
Right Aortic Arch and Double Aortic Arch.—See pages 442 and 444.
Transposition of the Aorta and Pulmonary Artery.—See page 448.
Persistent Truncus Arteriosus.—See page 449
Coarctation of the Aorta.—See page 457.
Patent Ductus Arteriosus.—See page 466.

DISPLACEMENT OF THE HEART

Moderate displacement of the heart can occur with pneumothorax, large pleural effusions, intrathoracic masses. Kyphoscoliosis not only causes displacement but can greatly distort the cardiac shadow (page 632). A funnel chest, if marked, may displace the heart to the left.

ABNORMAL FINDINGS ON ROENTGENKYMOGRAPHIC AND ELECTROKYMOGRAPHIC EXAMINATION

I have already mentioned that paradoxical pulsations may occur after myocardial infarction However, such paradoxical systolic expansile pulsations may occur in the absence of myocardial infarction Characteristic pulsations are also noted in the electrokymogram in constrictive pericarditis (page 652) For the effect of valvular lesions on the electrokymogram, the reader is referred to original papers on the subject The roentgenkymogram has also been used to differentiate aortic aneurysms from mediastinal tumors. However, an aortic aneurism may show no pulsation, whereas a mediastinal tumor may show large pulsations, transmitted from the aorta.

ABNORMAL FINDINGS ON ANGIOCARDIOGRAPHIC EXAMINATION

I have already mentioned that moderate enlargement of the right ventricle which is not sufficient to cause appreciable changes in a conventional x-ray film of the chest may show curvature of the interventricular septum to the left instead of to the right on angiocardiographic examination. The angiocardiographic pattern of interauricular septal defects is described on page 407, tetralogy of Fallot, on page 419, the Eisenmenger complex, on page 415, congenital isolated pulmonary stenosis, on page 426, coarctation of the aorta, on page 458; patent ductus arteriosus, on page 466; pericardial effusion, on page 645. Angiocardiography has also proven of value in the diagnosis of syphilitic aortitis (page 543), aneurisms of the aorta and

pulmonary artery, dissecting aneurism of the aorta (page 661), obstruction of the supérior vena cava, anomalous pulmonary veins draining into the right heart, dextrocardia, transposition of the great vessels, right aortic arch, *etc.*

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CONGENITAL ABNORMALITIES OF THE HEART AND GREAT VESSELS

Dextrocardia.—See pages 398 and 400.
Interauricular Septal Defects.—See page 406.
Interventricular Septal Defects.—See page 411.
Eisenmenger Complex.—See page 413.
Tetralogy of Fallot.—See page 418.
Dextroposition of the Aorta.—See page 415.
Congenital Pulmonary Stenosis.—See page 426
Tricuspid Atresia.—See page 431.
Right Aortic Arch and Double Aortic Arch.—See pages 442 and 444.
Transposition of the Aorta and Pulmonary Artery.—See page 448
Persistent Truncus Arteriosus.—See page 449
Coarctation of the Aorta.—See page 457.
Patent Ductus Arteriosus.—See page 466.

DISPLACEMENT OF THE HEART

Moderate displacement of the heart can occur with pneumothorax, large pleural effusions, intrathoracic masses. Kyphoscoliosis not only causes displacement but can greatly distort the cardiac shadow (page 632). A funnel chest, if marked, may displace the heart to the left.

ABNORMAL FINDINGS ON ROENTGENKYMOGRAPHIC AND ELECTROKYMOGRAPHIC EXAMINATION

I have already mentioned that paradoxical pulsations may occur after myocardial infarction. However, such paradoxical systolic expansile pulsations may occur in the absence of myocardial infarction. Characteristic pulsations are also noted in the electrokymogram in constrictive pericarditis (page 652). For the effect of valvular lesions on the electrokymogram, the reader is referred to original papers on the subject. The roentgenkymogram has also been used to differentiate aortic aneurisms from mediastinal tumors. However, an aortic aneurism may show no pulsation, whereas a mediastinal tumor may show large pulsations, transmitted from the aorta

ABNORMAL FINDINGS ON ANGIOCARDIOGRAPHIC EXAMINATION

I have already mentioned that moderate enlargement of the right ventricle which is not sufficient to cause appreciable changes in a conventional *x*-ray film of the chest may show curvature of the interventricular septum to the left instead of to the right on angiocardiographic examination. The angiocardiographic pattern of interauricular septal defects is described on page 407, tetralogy of Fallot, on page 419; the Eisenmenger complex, on page 415, congenital isolated pulmonary stenosis, on page 426; coarctation of the aorta, on page 458; patent ductus arteriosus, on page 466, pericardial effusion, on page 645. Angiocardiography has also proven of value in the diagnosis of syphilitic aortitis (page 543), aneurisms of the aorta and

Chapter 10

ABNORMAL ELECTROCARDIOGRAPHIC FINDINGS

THE normal electrocardiogram is described on page 82.

Abnormalities of the Heart Rate and the Cardiac Arrhythmias.—See Chapters 18, 19, 20

Abnormalities of the P Wave.—Large, wide *P* waves indicate auricular hypertrophy, page 209. Small *P* waves have no significance Variations in the direction or position of *P* are described in Chapter 18, page 316

Abnormalities of the P-R Interval.—The prolonged *P-R* interval is discussed on page 324. A short *P-R* interval of 0.10 second or less may occur normally. However, it is also present in the Wolff-Parkinson-White syndrome, page 375 A short *P-R* interval also occurs in nodal rhythm, page 322, but here, the abnormal shape of the *P* indicates that nodal rhythm is present.

Abnormalities of the QRS Complex.—High voltage is described on page 210 Low voltage of the *QRS* is present when the amplitude of *QRS* is less than 5 mm in all three standard leads or all three augmented unipolar extremity leads. It may occur normally but it can be produced by pericardial effusion or fluid accumulation in any of the body cavities, in myocardial infarction, scleroderma, myxedema, *etc.* A diagnosis of heart disease should *not* be made by the presence of low voltage alone, unless abnormalities of the *Q*, *RS-T* or *T* are also present.

Electrical Alternans.—Electrical alternans exists when *QRS* complexes of a given amplitude alternate with *QRS* complexes of another amplitude. Alternans of the *T* may also be present. It usually indicates serious heart disease It should not be confused with the rhythmic and progressive alterations in the amplitude of the *QRS* and *T* due to respiration Electrical alternans may or may not be associated with pulsus alternans (page 142).

Prolongation of the QRS Interval.—Prolongation of the *QRS* interval to 0 12 second or more occurs not only in bundle branch block (Chapter 21, page 372), and in other forms of intraventricular conduction disturbance, but in cases of left ventricular hypertrophy, rarely right ventricular hypertrophy, and in ventricular premature contractions and ventricular tachycardia.

Abnormal Q Waves.—The presence of a *Q* wave is not necessarily a sign of heart disease However, abnormal *Q* waves may appear after myocardial infarction The following criteria can be used to determine whether a *Q* is normal or abnormal, that is, due to myocardial infarction:

Abnormal Q Waves in Precordial Leads.—When infarction of the anterior wall of the heart occurs, abnormal *Q* waves with the following characteristics may develop in precordial leads $V_{3,4,5,6}$:

1. The depth of *Q* is 25 per cent or more the amplitude of the *R* wave; or the entire *QRS* complex may consist of a *QS* deflection.

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Abnormal Findings on Roentgenkymographic and Electrokymographic Examination

Also see page 78

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1. A Q wave is also present in lead II, and is approximately 25 per cent the amplitude of R_2.
2. The depth of Q_3 is 50 per cent or more the amplitude of the tallest R in the standard leads.
3. The width of Q_3 is 0 04 second or more.
4. Lead I has no S wave or a small s.

Abnormal RS-T Segments.—Abnormalities of the *RS-T* segment may occur in ventricular strain, bundle branch block, myocardial anoxemia, myocardial infarction, pericarditis, trauma to the heart, myocarditis, malignancy of the heart; as a result of digitalis, quinidine, epinephrine, insulin, and other drugs; in hypopotassemia due to diabetic acidosis or persistent vomiting, or other causes, with changes of posture to a sitting or standing position, and in many other ways.

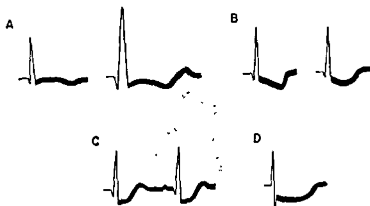


FIG 51 —Diagrams showing the characteristics of abnormal, depressed *RS-T* segments *A*, Left ventricular strain, and left ventricular hypertrophy and strain *B*, Digitalis effects *C*, Myocardial anoxia or acute coronary insufficiency. *D*, Myocardial injury (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed , 1953.)

RS-T Depressions (Fig 51) —Some of the more characteristic types of *RS-T* depressions are the following.

Ventricular Strain.—Moderate changes consist in slight depression of the *RS-T* with a downward *T*. When the changes are marked, the depressed *RS-T* shows an upward bowing, and the downward *T* rises above the base line and then returns to the base line, giving a "roller-coaster" appearance (Fig. 51, *A*).

Digitalis Effects —The depressed *RS-T* may run obliquely downward, fuse with the lowest point of *T* which then abruptly returns to the base line (Fig 51, *B*). A variation of this pattern is the hollow, or scooped-out appearance of the *RS-T* (Fig. 51, *B*). The *Q-T* interval is also shortened.

Myocardial Anoxia (Acute Coronary Insufficiency).—A sharply depressed *RS-T* rises abruptly to the base line. The final portion of *T* may be upward (Fig. 15, *C*). A sinus tachycardia is often present.

Myocardial Injury.—The depressed *RS-T* seems to be elongated, due to prolongation of the *Q-T* interval (Fig. 51, *D*). It often shows a downward bowing.

2. The width of Q is 0.04 second or more. (The width of Q is measured on the upper level of the base line from the point where Q begins to the point where Q returns to the base line

An abnormal QS pattern may appear in lead V_1, or leads $V_{1,2}$, in association with the abnormal Q waves described above. However, lead V_1 often show a QS normally. In such a case, the precordial lead immediately to the left shows an rS pattern Once an rS pattern appears in a precordial lead, a QS in a precordial lead to the left is always abnormal, even it it occurs in lead V_2. An abnormal QS in leads $V_{1,2}$ is usually slurred or notched, in contrast to a normal QS in these leads.

When left bundle branch block, or left ventricular hypertrophy and strain are present, a QS may appear in leads $V_{1,2,3}$ in the absence of myocardial infarction. In such cases also, the lead immediately to the left shows an rS.

Precordial lead V_1, and rarely leads $V_{1,2}$ may also show a qR pattern in the absence of infarction, when extreme clockwise rotation of the heart is present. In such cases, the precordial lead immediately to the left shows an rS, or a tall R. (The presence of such a pattern is a sign of right ventricular hypertrophy)

Abnormal Q Wave in Lead aVL.—This has the following characteristics:

1. A QR pattern is present in lead aVL, and the depth of Q is 50 per cent or more the amplitude of R.
2. Q_{aVL} is 0.04 second or more wide.
3. P_{aVL} is upward.
4. Lead aVR shows an rS pattern.

Lead aVL may also show a QS after myocardial infarction, but a similar pattern may occur normally. However, an abnormal QS_{aVL} is usually notched, is associated with an upward P, and usually with an abnormal $RS\text{-}T$ segment or T wave

Lead aVL may show a QR with a deep wide Q wave after myocardial infarction, but lead aVR shows a QR or Qr, or qR pattern instead of an rS pattern A similar pattern may also occur normally. In such cases, the precordial leads will also show abnormal Q waves if myocardial infarction is present.

Abnormal Q Wave in Lead aVF.—This has the following characteristics:

1. The depth of Q is 60 per cent or more the amplitude of R A QS may be present.
2. The width of Q is 0.04 second or more
3. Lead aVR shows an rS or a QS, but not a Qr, QR or a qR.

Occasionally, when criteria 2 and 3 are present, the depth of Q is only 25 per cent that of R or less

Abnormal Q Wave in Lead I.—This is produced by the abnormal Q in lead aVL. (Lead I equals left arm—right arm). It has the following characteristics

1. An R is present in lead I, but is small, approximately 5 mm.
2. Q is at least 1 mm. deep.
3. Q is 0.04 second or more wide

Abnormal Q Wave in Lead III.—This is produced by the abnormal Q in lead aVF. (Lead III equals left leg—left arm). It has the following characteristics:

and many other conditions can produce flat *T* waves or a reversal of the direction of *T*. One must therefore be very cautious in stating that an electrocardiogram that shows only abnormalities of *T* is a sign of heart disease, because abnormal *T* waves can appear in so many conditions in which the heart is normal.

It appears that many, if not most of these changes are related to the concentration of potassium and calcium in the heart muscle and in the blood. The concentrations of potassium and calcium vary independently of each other and in any case, determinations of both these electrolytes should be done if accurate correlations with the electrocardiogram are to be made The most important of these changes will now be considered

Potassium and the Electrocardiogram.—Potassium is probably the most important electrolyte in the body because it apparently governs the shape, amplitude and direction of the *T* and *U* waves and can also cause variations in the *RS–T* segment and *Q–T* interval. Numerous reports have been published showing how changes in the *RS–T* and *T* can be correlated

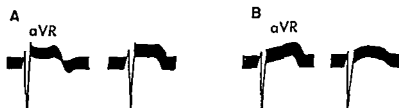


FIG 53 —Diagrams showing abnormal *RS–T* elevations in lead *aVR* *A*, Myocardial anoxia (acute coronary insufficiency) *B*, Digitalis effects (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed, 1953)

with blood potassium levels However, the correlation has not been perfect because the potassium content of heart muscle (and other cells) may be low when the blood serum potassium level is high, and vice versa Unfortunately, it is not possible to measure intracellular potassium levels by any simple method, so that instead of correlating the electrocardiogram with heart muscle potassium levels, we are forced to rely on the less accurate correlation of the electrocardiogram with the level of potassium in the blood serum.

Hypopotassemia (Hypokalemia).—Assuming that there are no local alterations of the potassium content of heart muscle (due to muscle injury or ventricular strain, etc), the electrocardiographic changes which occur in hypopotassemia can be correlated in a general way with the level of potassium in the serum Normally, the serum potassium level varies from 3 5 to 5 mEq./L (milliequivalents per liter) (14 to 20 mg /100 cc.), and significant electrocardiographic changes usually appear when the level drops to 3 mEq /L or lower

The term, *milliequivalents per liter* (mEq /L.) is replacing the conventional term, milligrams per cent (mg /100 cc.) because it allows accurate

RS–T Elevations.—When the *RS–T* depressions described above occur in lead *aVL* or in lead I, reciprocal *RS–T* elevations usually appear in lead *aVF* or in lead III. However, significant *RS–T* elevations, indicative of myocardial injury, may appear in any of these leads The *RS–T* deviations due to injury can be described as follows:

The Plateau RS–T —The *RS–T* begins above the base line, runs straight and horizontally, fuses with the *T* and gradually descends to the base line (Fig 52, *A*)

The Dome-Shaped RS–T —The *RS–T* begins above the base line and continues to rise with an upward convexity. As it begins to descend it fuses with the *T* (Fig. 52, *B*).

The Obliquely Elevated RS–T —The *RS–T* begins above the base line, and continues to rise obliquely. It fuses with the peak of the *T* and rapidly descends to the base line (Fig. 52, *C*).

The Crescent RS–T —The *RS–T* begins above the base line, descends in a gentle slope and then turns and rises to fuse with the peak of an upward

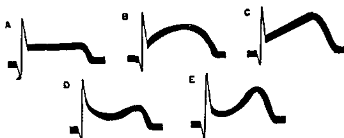


Fig 52—Diagrams showing abnormally shaped, elevated *RS–T* segments *A*, Plateau *RS–T* *B*, Dome-shaped *RS–T* *C*, Obliquely elevated *RS–T*. *D*, Crescent *RS–T* *E*, Abnormally elevated *RS–T* with a normal shape (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed, 1953)

T. The result is an inverted dome or crescent. The lowest point or nadir of the *RS–T* is equidistant from the beginning of the *RS–T* and the peak of *T* (Fig 52, *D*).

Frequently after myocardial injury, the elevated *RS–T* has one of these abnormal shapes, even though its elevation is statistically within normal limits. Occasionally, the elevated *RS–T* maintains its normal downward bowing in spite of the presence of myocardial injury (Fig. 52, *E*) but in such cases, it shows a statistically significant elevation (Table 1, page 85).

Figure 53 shows significant *RS–T* elevations which may occur in lead *aVR*

Abnormal T Waves.—The conditions that produce changes in the *T* waves are even more numerous than those which produce *RS–T* deviations, and are less well understood. Eating, changes in posture, malnutrition, fear, drugs such as digitalis, quinidine, epinephrine, ephedrine, atropine, tobacco, desoxycorticosterone, etc., myocarditis, pericarditis, acute infections of any etiology, uremia; endocrine disturbances such as Addison's disease, Cushing's syndrome, Simmonds' disease, myxedema, diabetic acidosis;

prolonged in such cases However, the prolongation may be more apparent than real because it may be difficult to determine where the *T* ends and the *U* begins. As a consequence, the *Q–U* interval, rather than the *Q–T* interval, is often measured

3 Downward *T* waves and prominent *U* waves (Fig. 54*D*, *E*, *F*) Such a pattern is best seen in precordial leads, such as V_1 through V_4 which overlie the right ventricle and thus have an *rS* or *RS* pattern.

4. Depression of the *RS–T* segment and slight lengthening of the *Q–T* interval (Fig. 54*D*, *E*). The *RS–T* may be slightly depressed or may show several small undulations (Fig. 54*C*). Figure 54*D*, *E*, *F*, *G*, show more marked *RS–T* deviations. These *RS–T* segments have a sagging appearance, characteristic of hypopotassemia.

5. A prolonged *P–R* interval may also occur with any of these patterns.

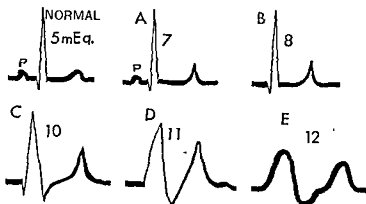


Fig 55 —Hyperpotassemia (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger)

Although Figure 54*A*, through *G* shows the progressive changes which can occur as hypopotassemia becomes more marked, these progressive changes do not always occur, and it may be impossible to determine the exact degree of hypopotassemia from the electrocardiogram

Hyperpotassemia (Hyperkalemia) —The electrocardiographic changes which occur with hyperpotassemia can be related in a general way to the level of serum potassium.

At a level of approximately 7 mEq /L, tall, peaked *T* waves with a narrow base occur (Fig. 55*A*)

At approximately 8 mEq /L, the *P* waves may disappear or wander in and out of the *QRS* (Fig 55*B*).

At approximately 10 mEq /L., wide, aberrant *QRS* complexes appear (Fig. 55*C*).

At approximately 11 mEq /L, biphasic deflections, caused by a fusion of the *QRS* complex, *RS–T* segment and the *T* wave, appear (Fig 55*D*)

comparisons of electrolyte balances to be made. The relation between mEq /L. and mg./100 cc. is as follows.

$$\text{mEq /L} = \frac{\text{mg./100 cc.} \times 10 \times \text{valence}}{\text{atomic weight}}$$

Milligrams per cent can be converted to milliequivalents per liter in the following way.

For potassium, divide mg./100 cc by the factor, 4, to get mEq./L. (Or multiply mEq./L. by 4 to get mg./100 cc.).

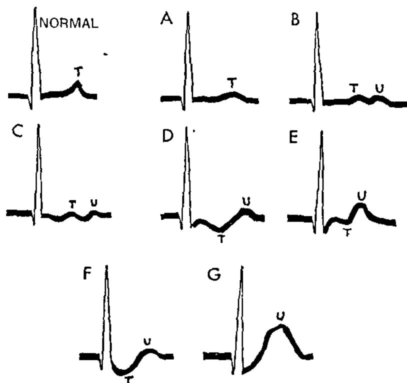


FIG 54 —Hypopotassemia (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger)

For calcium, divide mg./100 cc by the factor, 2, to get mEq./L (Or multiply mEq./L. by 2 to get mg./100 cc).

Figure 54 shows some of the common changes seen in hypopotassemia. The changes include:

1 Lowering and broadening of the *T* wave (Fig. 54*A*). The *Q–T* interval is also slightly prolonged. Such a pattern may occur when the serum potassium is merely at a low normal level, for example, 3 5 mEq./L.

2 Low, broad *T* waves with a double summit, due to superimposition of the *U* wave on the *T* (Fig. 54*B*). The *Q–T* interval may appear markedly

prolonged in such cases However, the prolongation may be more apparent than real because it may be difficult to determine where the *T* ends and the *U* begins As a consequence, the *Q–U* interval, rather than the *Q–T* interval, is often measured.

3. Downward *T* waves and prominent *U* waves (Fig. 54*D*, *E*, *F*). Such a pattern is best seen in precordial leads, such as V_1 through V_4 which overlie the right ventricle and thus have an *rS* or *RS* pattern.

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5. A prolonged *P–R* interval may also occur with any of these patterns.

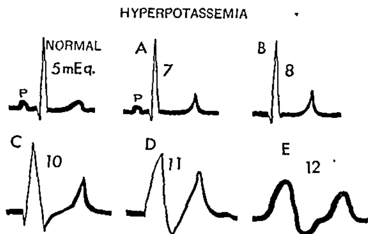


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At approximately 8 mEq./L , the *P* waves may disappear or wander in and out of the *QRS* (Fig 55*B*)

At approximately 10 mEq./L., wide, aberrant *QRS* complexes appear (Fig 55*C*).

At approximately 11 mEq /L , biphasic deflections, caused by a fusion of the *QRS* complex, *RS–T* segment and the *T* wave, appear (Fig 55*D*).

At 12 mEq./L., (or even at a lower level of 10 mEq./L.) ventricular fibrillation or cardiac standstill and death may occur (Fig. 55E).

With the onset of the wide, aberrant *QRS* complexes and the loss of the *P* waves, an idioventricular rhythm develops (similar to that seen in complete *a–v* block). The ventricular rate may be regular, irregular, slow or rapid, and the tracing may resemble even a ventricular tachycardia. In addition, the shape of the abnormal *QRS* complexes may vary from beat to beat.

CALCIUM AND THE ELECTROCARDIOGRAM

Both hypocalcemia and hypercalcemia can cause changes in the *RS–T* segment and the *Q–T* interval. However, changes in serum calcium often occur simultaneously with changes in serum potassium, and in a particular case, if hypopotassemia or hyperpotassemia is present, the electrocardio-

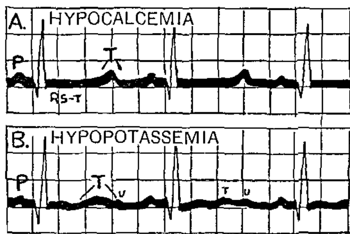


FIG. 56.—Hypocalcemia compared to hypopotassemia. (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger.)

gram will indicate the potassium, rather than the calcium abnormalities. This is the reason that blood calcium determinations should be done on every case of hypo- and hyperpotassemia.

The normal blood calcium level is from 4.5 to 5.5 mEq./L. (9 to 11 mg./100 cc.). Changes in the electrocardiogram usually appear when the level falls below 3.5 mEq./L. (7 mg./100 cc.) or rises above 6 mEq./L. (12 mg./100 cc.).

Hypocalcemia.—When hypocalcemia occurs, the *RS–T* segment becomes lengthened and the *Q–T* interval becomes prolonged. However, the *T* wave will remain more or less normal, if the blood potassium level is within normal (Fig. 56*A*). Such prolongation of the *Q–T* interval due to hypocalcemia can be differentiated from that due to hypopotassemia, because in hypopotassemia the prolongation of the *Q–T* is due to widening of the *T* wave rather than to a lengthening of the *RS–T* segment (Fig. 56*B*). However, if hypocalcemia occurs in association with hypopotas-

semia, as may occur, for example, in sprue, celiac disease, acute pancreatitis, during the course of replacement transfusions in infants, alkalosis, uremia, hepatic coma, etc., the *Q–T* interval will be prolonged due to the hypocalcemia, but the *T* wave will be flat and wide and the tracing will be indicative of hypopotassemia rather than hypocalcemia.

Hypercalcemia.—In hypercalcemia, the *Q–T* interval is usually short and the *Q–T* ratio frequently less than 1. The shortened *Q–T* is due to shortening of the *RS–T* segment. If the blood potassium level is normal, as may occur in hyperparathyroidism, the *T* waves will be normal. However, if the blood potassium level is low for any reason, the *Q–T* will become prolonged, the *T* waves will become wide and flat and the tracing will be typical of hypopotassemia rather than hypercalcemia.

In addition to hyperparathyroidism, large doses of testosterone or estrogens, especially if given to bed-ridden patients, or para-aminosalicylic acid, or vitamin D can cause hypercalcemia. It can also occur in renal rickets, etc.

Other Electrolytes.—It is possible that in addition to potassium and calcium, changes in blood magnesium or sodium may cause *RS–T* and *T* changes. In addition, acidosis and alkalosis may cause electrocardiographic changes not related to a concomitant shift in potassium or calcium levels.

Abnormal Q–T Interval.—Abnormal prolongation of the *Q–T* interval occurs in ventricular strain, myocardial infarction (but not pericarditis with effusion), bundle branch block, hypopotassemia and hypocalcemia, rheumatic fever, scarlet fever, and other infections. The prolonged *Q–T* interval of hypopotassemia is largely due to a widening of the *T* wave, whereas in hypocalcemia the prolonged *Q–T* is due to a lengthening of the *RS–T* segment. Quinidine may also prolong the *Q–T* interval. Digitalis causes a shortening of the *Q–T* interval. A short *Q–T* interval is also usually found in hypercalcemia.

Auricular Hypertrophy.—Auricular hypertrophy can be suspected when the *P* in any of the augmented unipolar extremity leads or standard leads has a width of 0.11 second or more and an amplitude of 2.5 mm. or more, or when the *P* in precordial lead V_1, or V_2 is more than 2 mm. large. However, auricular hypertrophy may be present with normal *P* waves. There is no exact method of determining from the electrocardiogram whether right or left auricular hypertrophy is present. However, when right auricular hypertrophy occurs, very large biphasic *P* waves appear in precordial leads $V_{1,2}$.

Tall thin *P* waves in lead *aVF* and leads II and III (*P pulmonale pattern) often occur in patients with cor pulmonale.* However, such *P* waves may occur in normal people.

Ventricular Hypertrophy and Strain.—A distinction should be made between the electrocardiographic effects of ventricular hypertrophy and strain. Ventricular hypertrophy causes primary changes in the *QRS* complex, with high voltage of the *QRS* with or without widening of the *QRS*. Ventricular strain produces *RS–T* and *T* changes. Although strain is often present in patients who have ventricular hypertrophy, it may occur in an otherwise normal heart. The exact method by which ventricular strain produces

electrocardiographic changes is unknown. There is some evidence that the changes are due to a loss of potassium from either the right or the left ventricle.

Left Ventricular Strain.—In leads that overlie or face the epicardial surface of the strained left ventricle, a qR pattern appears with a depressed RS–T and downward T (see page 203 for characteristics of the RS–T). Left ventricular strain usually occurs in patients with hypertensive cardiovascular disease, but it can occur as a result of drugs such as epinephrine, during the course of acute infections, and in other ways in persons with normal hearts.

Left Ventricular Hypertrophy.—Left ventricular hypertrophy may be present with a normal electrocardiogram. However, high voltage of the QRS

LEFT VENTRICULAR HYPERTROPHY AND STRAIN

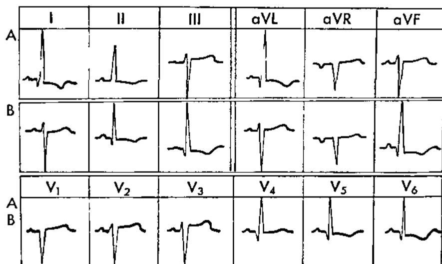


FIG. 57.—Left ventricular hypertrophy and strain. The tall QRS complexes indicate the left ventricular hypertrophy. The RS–T and T deviations indicate the ventricular strain. *A*, The heart is horizontal. *B*, The heart is vertical.

may result. When a tracing shows one of the following criteria for high voltage, left ventricular hypertrophy can be diagnosed:

Lead aVL.—A qR pattern is present and R is 13 mm. or more tall.

Lead aVF.—A qR pattern is present and R is 20 mm. or more tall.

Lead I shows a qR pattern and the sum of R_1 and S_3 is more than 25 mm.

Lead III shows a qR pattern and the sum of R_2 and R_3 is more than 40 mm.

Criteria for high voltage in the precordial leads are difficult to determine. However, if the sum of R in lead V_5 or V_6 and S in lead V_1 or V_2 exceeds 35 mm., this also is suggestive of left ventricular hypertrophy.

Left Ventricular Hypertrophy and Strain (Fig. 57).—Here the tracing shows high voltage of the QRS, due to left ventricular hypertrophy and RS–T and T deviations due to left ventricular strain. There is often

widening of the QRS and marked RS–T and T deviations. In leads with an rS pattern, marked elevation of the RS–T may appear with upward T waves. The augmented unipolar extremity leads and standard leads vary depending on whether the heart is horizontal or vertical.

This pattern usually appears in patients with advanced hypertensive cardiovascular disease, or chronic nephritis.

Right Ventricular Strain (Fig. 58).—Downward T waves appear in precordial leads which overlie and face the right ventricle. Thus, an rS or RS and downward T may appear in leads V_1 through V_3 or V_4. Since there is marked clockwise rotation of the heart, lead aVR shows a Qr, QR or qR pattern.

Acute right ventricular strain may occur after pulmonary embolism, left-sided heart failure, and widespread pneumonia. Chronic right ventricular strain usually occurs in patients with chronic cor pulmonale or congenital heart disease involving the right ventricle.

RIGHT VENTRICULAR STRAIN

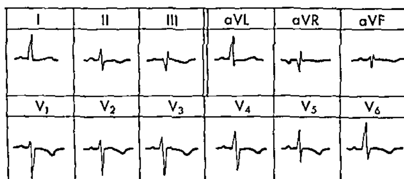


Fig 58.—Right ventricular strain

Right Ventricular Hypertrophy (Fig 59).—Right ventricular hypertrophy may exist with a normal electrocardiogram. However, tall R waves with downward T waves may develop in precordial lead V_1 or leads $V_{1,2}$, which overlie or face the hypertrophied right ventricle. The peak of the R wave (time of onset of the intrinsicoid deflection) occurs from 0.03 to 0.05 second after the beginning of the QRS. There is usually marked clockwise rotation, so that lead aVR shows a Qr, QR or qR. The clockwise rotation may be so extreme, that precordial lead V_1 or leads $V_{1,2}$ also show a qR pattern (see page 202). The position of the heart is usually vertical. This is reflected in the patterns of leads aVL, aVF and the standard leads.

Vectorcardiographic studies have resulted in another criterion of right ventricular hypertrophy, namely, that the peak of R in lead V_1 occurs later than the peak of R in lead I (see page 92).

Bundle Branch Block.—See page 372.

Myocardial Injury.—Myocardial injury can be produced by trauma, pericarditis, occlusion of a coronary artery, or a sudden decrease in coro-

electrocardiographic changes is unknown. There is some evidence that the changes are due to a loss of potassium from either the right or the left ventricle.

Left Ventricular Strain.—In leads that overlie or face the epicardial surface of the strained left ventricle, a qR pattern appears with a depressed $RS-T$ and downward T (see page 203 for characteristics of the $RS-T$). Left ventricular strain usually occurs in patients with hypertensive cardiovascular disease, but it can occur as a result of drugs such as epinephrine, during the course of acute infections, and in other ways in persons with normal hearts.

Left Ventricular Hypertrophy.—Left ventricular hypertrophy may be present with a normal electrocardiogram. However, high voltage of the QRS

LEFT VENTRICULAR HYPERTROPHY AND STRAIN

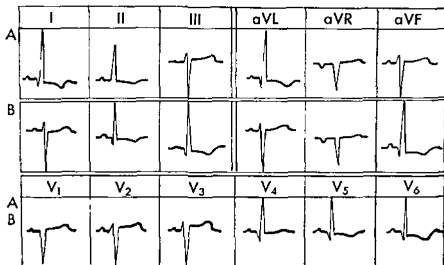


Fig 57 —Left ventricular hypertrophy and strain The tall QRS complexes indicate the left ventricular hypertrophy The $RS-T$ and T deviations indicate the ventricular strain A, The heart is horizontal B, The heart is vertical

may result. When a tracing shows one of the following criteria for high voltage, left ventricular hypertrophy can be diagnosed:

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Lead III shows a qR pattern and the sum of R_2 and R_3 is more than 40 mm.

Criteria for high voltage in the precordial leads are difficult to determine. However, if the sum of R in lead V_5 or V_6 and S in lead V_1 or V_2 exceeds 35 mm., this also is suggestive of left ventricular hypertrophy.

Left Ventricular Hypertrophy and Strain (Fig. 57).—Here the tracing shows high voltage of the QRS, due to left ventricular hypertrophy and $RS-T$ and T deviations due to left ventricular strain. There is often

waves have been described on page 201. They usually persist indefinitely after the infarct, but rarely may disappear.

Pericarditis.—See page 615.
Anterior Infarction.—See page 597.
Posterior Infarction.—See page 598.
Myocardial Anoxia (Acute Coronary Insufficiency).—See page 297
Pulmonary Embolism.—See page 620.

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(Also see page 93, and references under various diseases)

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nary artery flow, even without coronary artery occlusion, or by a tumor invading the heart, or a gumma, *etc.* Regardless of the nature of the injurious agent, characteristic *RS–T* elevations occur in one or more leads as a sign of the myocardial injury (see page 204). Reciprocal depression of the *RS–T* occurs in leads that face uninjured surfaces of the heart, but the *RS–T* elevations are more important in diagnosis because they appear in leads that directly face the surface of the injured muscle. In most cases of myocardial injury, a portion of the epicardial surface of the heart is injured, either directly or from extension of injury within the muscle depths. Thus, depending on the size and location of the injured area, and the position of the heart, one or more of the precordial leads, or lead *aVL* or *aVF*, or one or more of the standard leads will show characteristic elevation of the *RS–T*. When the endocardium is injured, as occurs in acute myocardial anoxemia (acute coronary insufficiency), or in subendocardial infarction lead *aVR*, which faces the cavity of the heart, shows the elevated *RS–T*.

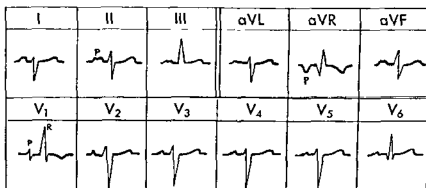


FIG 59 —Right ventricular hypertrophy

In most cases, the *RS–T* deviations return to the base line after a variable period of time (days, weeks, months or longer) and abnormal *T* waves develop Leads which showed elevated *RS–T* segments develop deep symmetrical *T* waves (The *T* wave is symmetrical because its peak lies midway between the beginning and the end of *T* (Figs 103, page 597; 104, page 599) unlike the normal asymmetrical *T* wave (Fig. 22, *C*, page 82). After another variable period of time these *T* waves reach a maximum, then decrease in amplitude and finally become normal (Fig. 103, page 597; Fig. 104, page 599). Thus the tracing may completely return to normal after myocardial injury However, if in addition to myocardial injury, a large portion of the muscle dies, abnormal *Q* waves will also develop in leads that face the surface of the injured area. This usually occurs in cases of myocardial infarction due to coronary artery occlusion, but may occur after trauma, if a coronary artery is severed, or with coronary artery embolism, *and may even occur with a decrease in coronary artery flow if the area of* muscle death is large enough. The characteristics of these abnormal *Q*

ever, *Grade 1* and occasionally *Grade 2* abnormalities are occasionally found even in such persons.

After the age of forty years, abnormal ballistocardiographic patterns of *Grade 2* or more are common in otherwise normal persons.

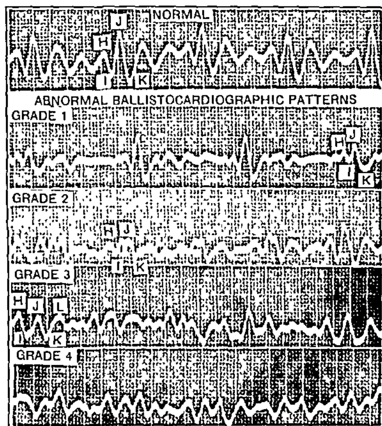


FIG 60 — Abnormal ballistocardiographic patterns See text for details

ABNORMALITIES OF AMPLITUDE

This can be measured accurately only by instruments which can be calibrated

Abnormally *large complexes* occur in cases where the cardiac output tends to be high, as in hyperthyroidism, arteriovenous fistulas, severe anemia and some forms of chronic pulmonary disease Large complexes are also found in aortic insufficiency, some cases of neurocirculatory asthenia and in emotional states such as excitement. The amplitude may also increase physiologically after eating, after exercise and during anoxemia

Abnormally *small complexes* occur in heart failure, coronary artery disease, in conditions with a low cardiac output, such as myxedema, and in pericarditis, hypertensive heart disease and other forms of heart disease

Chapter 11

ABNORMAL BALLISTOCARDIOGRAPHIC FINDINGS

INTRODUCTION

THE interpretation of ballistocardiograms is difficult for many reasons. First, tracings are taken with various types of ballistocardiographic apparatus, as has already been mentioned Secondly, it is difficult, and at times impossible to standardize the apparatus. Thirdly, the full range of normal variations is not yet known. In addition, nonspecific abnormalities may occur if the patient lies on a couch which may dampen all or part of the waves, or the tracing may be taken immediately after a meal which can cause the waves to become larger or smaller; or the patient may be wearing a tight abdominal support, which can cause the waves to become smaller. Furthermore, abnormal ballistocardiographic patterns are not characteristic nor pathognomonic

It is for these and other reasons, that Dock and his associates recently wrote: "The ballistocardiographic record is read much as one reads the facies of a patient, it is not subjected to quantitative analysis, but is intuitively compared with the normal range for young adults and the variations noted by the observer or reported by others in groups of patients with specific diagnoses. . ."

There are many ways in which an abnormal ballistocardiogram can be described A simple, qualitative method, is as follows:

Ballistocardiograms are divided into four abnormal *grades:*

Grade 1 —Regularity and the definiteness of the waves are preserved. The inspiratory *IJ* amplitude is normal, but during expiration it decreases to one-half or less (Fig. 60).

Grade 2.—One-half or more of the waves are abnormal, again mainly during expiration (Fig 60)

Grade 3 —The waves in both inspiration and expiration show varying degrees of abnormality in regularity and definiteness. However, the waves are still individually identifiable The amplitude of all the waves is low (Fig. 60)

Grade 4 —Totally abnormal waves are present. These abnormal waves have a low amplitude, are irregular and the individual peaks and valleys are not identifiable (Fig. 60).

GENERAL ABNORMALITIES

It is generally agreed that a clinically normal person below the age of thirty-five or forty years, who has no condition known to affect the heart or circulation, almost invariably has a normal ballistocardiogram. How-

ever, *Grade 1* and occasionally *Grade 2* abnormalities are occasionally found even in such persons.

After the age of forty years, abnormal ballistocardiographic patterns of *Grade 2* or more are common in otherwise normal persons.

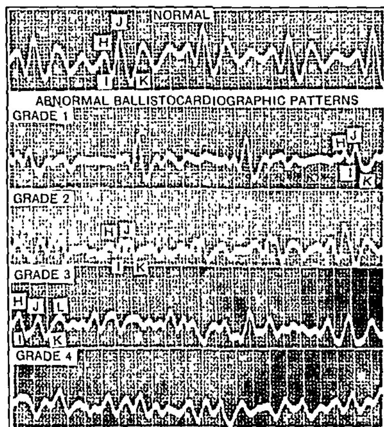


FIG 60 —Abnormal ballistocardiographic patterns See text for details

ABNORMALITIES OF AMPLITUDE

This can be measured accurately only by instruments which can be calibrated

Abnormally *large complexes* occur in cases where the cardiac output tends to be high, as in hyperthyroidism, arteriovenous fistulas, severe anemia and some forms of chronic pulmonary disease Large complexes are also found in aortic insufficiency, some cases of neurocirculatory asthenia and in emotional states such as excitement. The amplitude may also increase physiologically after eating, after exercise and during anoxemia

Abnormally *small complexes* occur in heart failure, coronary artery disease, in conditions with a low cardiac output, such as myxedema, and in pericarditis, hypertensive heart disease and other forms of heart disease.

ABNORMAL RESPIRATORY VARIATIONS OF THE BALLISTOCARDIOGRAM

On page 99, it was pointed out that the normal respiratory variations of the ballistocardiogram are due to the fact that on inspiration, the stroke volume of the right ventricle increases proportionately more than the stroke volume of the left ventricle decreases. Therefore, respiratory variations will be abnormally great in any condition which selectively interferes with the right ventricular output, or damages the left ventricle. Thus, an abnormal respiratory effect in the ballistocardiogram (the expiratory *IJ* stroke is one-half or less of its inspiratory value) can be seen in patients with pulmonary emphysema, or other chronic pulmonary lesions, and in cases of myocardial infarction, angina pectoris, or hypertensive heart disease. *Grade 1* abnormal respiratory variations can be produced by a normal person who hyperventilates

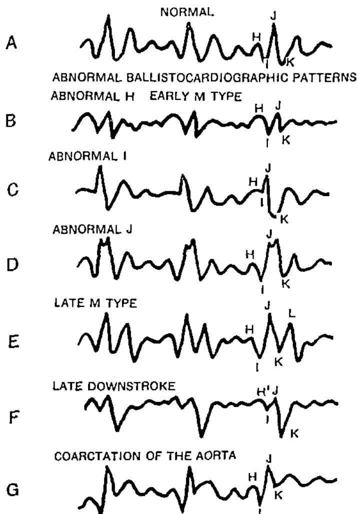


FIG 61A–G.—Abnormal ballistocardiographic patterns. See text for details.

ABNORMALITIES OF THE INDIVIDUAL WAVES

The following common abnormalities may be present:

1. The amplitude of *H* may become increased and equal to or exceed that of *J*. This will produce an "early *M*" (Fig 61*B*). This is most often seen in hypertension. It probably represents the increased size of the impact produced by the movement of the heart, which is trying to eject blood against an increased resistance However, the "early *M*" can occur in the absence of hypertension. It is not a serious finding.

2 The *I* wave may decrease in amplitude, or become poorly defined *I* can be considered abnormal if it is rounded, notched or flattened and if its area is markedly reduced (Fig. 61*C*).

3. *J* is abnormal if its peak is rounded, flattened or notched, so that it fails to dominate the record (Fig. 61*D*). A more advanced type of this abnormality has been called the "late *M*" type (Fig. 61*E*). When this occurs, it seems that the notch in the *J* has become bigger, extending even beneath the base line As a result, the *J* forms the first limb of the *M*.

One explanation for the "late *M*" is that one side of the heart is strong, the other weak. The stronger ejects blood in the normal way and produces maximum velocity of the ballistic wave early in systole, while the weaker side ejects blood with difficulty and does not produce maximum velocity until late in systole The "late *M*" type is serious.

4. There may be a combination of all of these abnormalities.

5. The *K* wave may be deep and broad (Fig 61*F*). This may become particularly obvious if the preceding *J* wave is low.

A short *HK* segment, with *K* remaining above the base line, may occur in coarctation of the aorta, aortic stenosis, hypertension, and in normal children (Fig. 61*G*).

6. The amplitude of *L* may be equal to or exceed that of the preceding *J*. Large *L* waves have been found in rheumatic carditis

7. Deep diastolic *M* waves may occur with a diastolic gallop

8 All the waves may produce a completely bizarre pattern.

Variable HK Interval.—The normal *HK* interval was described on page 100 Variations from beat to beat occur where the ballistic pattern is irregular and indefinite, as in cases of heart failure, myocardial infarction, or myocarditis.

CLINICAL CONDITIONS SHOWING ABNORMAL PATTERNS

Heart Failure.—The ballistocardiogram usually becomes abnormal in the presence of heart failure, regardless of the cause of the failure, and tends to return to normal as cardiac compensation is restored

In cases where the cardiac output is high (even when high-output heart failure is present, page 230), very large ballistic complexes are present, due to the high cardiac output. This is seen in cases of fever, arteriovenous fistulas, anemia, hyperthyroidism, emaciation, patent ductus arteriosus, and in some forms of chronic pulmonary disease On the other hand, in myxedema, pericarditis, and in other diseases associated with a low cardiac

output, the amplitude of the ballistocardiographic waves may be abnormally low

Large diastolic waves have been observed in gallop rhythm.

Congenital Heart Disease.—A short or absent *K* wave (Fig. 61*G*) has been consistently found in patients with coarctation of the aorta. This is to be expected because the amplitude of the *JK* stroke is a good clinical index of the functioning length of the aorta. The pattern tends to be obscured in cases of coarctation of the aorta associated with aortic insufficiency.

The short or absent *K* wave is *not* pathognomonic of coarctation of the aorta, because it has been observed in aortic stenosis and in cases of hypotension due to any cause. (This same pattern can also occur in a case of patent ductus, if a large volume of blood is shunted from the aorta to the pulmonary artery, thus decreasing the flow to the lower aorta.) The pattern tends to revert to normal after operation for the coarctation.

In some cases of patent ductus arteriosus, tetralogy of Fallot, and the Lutembacher syndrome, the complexes show a high amplitude due to a high cardiac output. Tall *L* waves may also appear However, these changes have no diagnostic significance

Rheumatic Heart Disease.—The changes which occur in rheumatic heart disease are for the most part nonspecific

Mitral Stenosis—High *N* waves have been reported in some cases of mitral stenosis as well as high *L* waves If auricular fibrillation is present, the pattern may become very abnormal, especially if the ventricular rate is rapid and irregular. The *H* wave tends to be small or absent in cases of auricular fibrillation, because the auricular component of the *H* is lacking.

Recently, a supposedly characteristic pattern of mitral stenosis has been described This consists of a slurred, doubled or otherwise deformed *I* wave

Aortic Stenosis.—A short *K* wave is often found in aortic stenosis (see page 218).

The *I* wave may be unusually wide and deep The reason for this is as follows: Normally, the ballistic effect of the expulsion of blood into the ascending aorta (which causes the *I* wave) is very rapidly succeeded by the counter effect of the impact of the ejected blood on the aortic arch This, together with the acceleration of the blood flow in the descending aorta produces the *J* wave. Retardation of the latter events in aortic stenosis causes the *I* wave to be less forcibly opposed ballistically. As a result, *I* becomes accentuated

Aortic Insufficiency.—Abnormally large complexes are found with short *I* waves and deep *K* waves in aortic insufficiency, regardless of whether it is due to syphilis or rheumatic heart disease.

Mitral Insufficiency—No characteristic changes have been noted.

Rheumatic Fever.—The ballistocardiogram may remain normal even in the presence of severe rheumatic carditis

Hypertensive Heart Disease.—The ballistocardiogram may remain normal in the presence of hypertensive heart disease. The first change which probably occurs is a deepening of the *K* wave, so that it greatly exceeds the depth of the *I* wave. (Normally both waves have a similar

output, the amplitude of the ballistocardiographic waves may be abnormally low.

Large diastolic waves have been observed in gallop rhythm.

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Aortic Insufficiency.—Abnormally large complexes are found with short *I* waves and deep *K* waves in aortic insufficiency, regardless of whether it is due to syphilis or rheumatic heart disease

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Chapter 12

ABNORMAL FINDINGS IN TESTS OF CIRCULATORY EFFICIENCY

ABNORMAL CARDIAC OUTPUT

THE normal values for the cardiac output are given on page 105

Decreased Cardiac Output.—A decreased cardiac output can occur in the following conditions. many cases of cardiac decompensation (also see page 230); paroxysmal tachycardia and auricular fibrillation, shock, occasionally, complete *a–v* block; constrictive pericarditis, and pericardial effusion with tamponade; myxedema.

Increased Cardiac Output.—An increased cardiac output occurs in the following conditions: hyperthyroidism (see page 682), anemia, beriberi, *a–v* fistula, and Paget's disease; chronic pulmonary disease (see page 628), pregnancy (see page 751); and some cases of cardiac decompensation (see page 230).

An increased cardiac output may also occur in cirrhosis of the liver In such a case, arterio-venous fistulas occur in the distorted liver architecture

ABNORMAL CIRCULATION TIME VALUES

Normal values for the arm-to-tongue and arm-to-lung circulation times are given on pages 106 and 107.

Prolonged Arm-to-Tongue Circulation Time.—Prolongation above twenty seconds of the arm-to-tongue circulation time occurs in the following conditions: most cases of left-sided heart failure, myxedema, polycythemia vera, some cases of complete *a–v* block; paroxysmal tachycardia The circulation time, however, is normal in patients with chronic pulmonary disease even if there is dyspnea. As cardiac compensation is restored, the circulation time returns to normal, and so can be used as a guide to therapy.

In pericardial effusion, the circulation time is normal or only slightly increased (below 20 seconds) despite an elevated venous pressure However, if there is an associated cardiac dilatation, as in rheumatic carditis with pericardial effusion, the circulation time will be greatly prolonged

Shortened Arm-to-Tongue Circulation Time.—A short circulation time of less than ten seconds occurs in conditions with an increased cardiac output such as hyperthyroidism, beriberi, anemia, *a–v* fistula, *etc* Even if heart failure occurs in such cases, the circulation time remains within normal limits. A normal person may also have an arm-to-tongue circulation time as low as eight seconds.

A short arm-to-tongue circulation time may also occur in patients with congenital heart disease and right-to-left (venous-arterial) shunts, such as

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ABNORMAL FINDINGS ON CARDIAC CATHETERIZATION

Normal values for the pressures within and the oxygen content of the cardiac chambers are given on page 113 and in Table 2. The following examples illustrate some of the uses of venous catheterization of the heart in the diagnosis of congenital heart disease:

1. If the superior vena cava has an oxygen content of 11.5 volumes per cent, and if the average right auricular oxygen content is 15 volumes per cent, but the oxygen content of the right ventricle is only 13 volumes per cent, it is a sign that oxygenated blood is entering the right auricle This is a presumptive sign of an interauricular septal defect (Also see page 350).

2. If the oxygen content of the right auricle is 12 5 volumes per cent, but that of the right ventricle and pulmonary artery 16 volumes per cent, it is a sign that oxygenated blood is entering the right ventricle This is a presumptive sign of an interventricular septal defect

3. If the oxygen content of the right auricle and right ventricle is 13 5 volumes per cent, but that of the pulmonary artery is 16 volumes per cent, it is a sign that oxygenated blood is entering the pulmonary artery. This is a presumptive sign of a patent ductus arteriosus

4 Measurement of the pressures in the right ventricle and pulmonary artery is also valuable because if the pressure in the right ventricle is definitely and constantly higher than that in the pulmonary artery, it is strongly suggestive of either a pulmonary stenosis or of idiopathic dilatation of the pulmonary artery.

Additional findings in some of the more common congenital abnormalities are presented in Table 2.

OXIMETRY

The oximeter is an instrument which measures the oxygen saturation of blood in the peripheral arteries by means of a photo-electric cell attached to the pinna of the ear. It has particular value in the diagnosis of congenital cardiac lesions, especially when used in connection with exercise and the measurement of the uptake of oxygen by the lungs

In a normal person, a standard exercise test, such as stepping up and down a step 20 cm high, 30 times in one minute, causes no decrease in the peripheral arterial oxygen saturation However, in congenital heart disease with a venous-arterial shunt, exercise will cause the arterial oxygen saturation to fall Such cases also show arterial oxygen unsaturation in the resting state, an abnormally prolonged time (more than one minute) to attain maximal saturation after breathing 100 per cent oxygen, and a failure to attain full arterial saturation on oxygen administration These findings indicate a venous-arterial shunt, but they do not indicate the site of the shunt (In cases with an arterio-venous shunt, the above findings do not occur)

The oxygen consumption per liter of ventilation can also be measured in association with oximetry tests (A Douglas bag can be used to collect the expired air and its oxygen content subsequently measured.) During exercise, a normal person will show an increase in the ratio of oxygen con-

the tetralogy of Fallot, *etc* In such cases, the test substance quickly reaches the systemic circulation because it short-circuits the lungs by passing through the shunt In such conditions, a double end-point may also occur. The second end-point is due to the normal passage of the test substance through the lungs and then into the systemic circulation.

A double end-point may also occur in a condition such as an interauricular septal defect where the shunt is from left-to-right rather than right-to-left In such a case, the injection of the test substance may transiently raise the pressure in the right auricle above that in the left auricle.

Prolonged Arm-to-Lung Circulation Time.—Prolongation above eight seconds occurs in conditions associated with an increased venous pressure such as right-sided heart failure, constrictive pericarditis or pericardial effusion with tamponade, obstruction of the superior vena cava, or of the veins of the upper extremity.

Shortened Arm-to-Lung Circulation Time.—Conditions associated with an increased cardiac output give a short arm-to-lung circulation time.

In cases of congenital heart disease with a right-to-left shunt, an interesting reaction occurs when the arm-to-lung circulation time is done. The ether passes through the shunt to the systemic circulation, producing tingling and stinging of the head and face and of the extremities at the same time as the ether appears on the breath.

ABNORMAL VENOUS PRESSURE FINDINGS

Normal values of the venous pressure are given on page 110.

When right-sided heart failure is present, there is a tendency for the venous pressure in the sitting position to be lower than in the lying position.

Generalized elevation of the venous pressure occurs in cases of right-sided heart failure, chronic constrictive pericarditis and pericardial effusion with tamponade. A moderate increase in venous pressure can occur with obstructive emphysema even though the heart is normal.

Elevation of the venous pressure in the upper extremities with a normal venous pressure in the lower extremities occurs with obstruction of the superior vena cava or of the innominate, subclavian or axillary veins. Elevation of the venous pressure in the lower extremities with a normal venous pressure in the upper extremities can occur from ascites, obstruction of the inferior vena cava, abdominal tumors, pregnancy, or thrombosis of the femoral or iliac veins

ABNORMAL VITAL CAPACITY FINDINGS

Normal values for the vital capacity are given on page 112. A decrease in vital capacity may occur in left-sided heart failure, or in pulmonary disease, or in diseases of the abdomen which interfere with the descent of the diaphragm (ascites, tumors, *etc.*). However, the vital capacity remains unchanged during pregnancy. The vital capacity is also low in any condition producing generalized weakness. This is the cause of the low vital capacity in hyperthyroidism.

ABNORMAL FINDINGS ON CARDIAC CATHETERIZATION

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2. If the oxygen content of the right auricle is 12.5 volumes per cent, but that of the right ventricle and pulmonary artery 16 volumes per cent, it is a sign that oxygenated blood is entering the right ventricle. This is a presumptive sign of an interventricular septal defect

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4. Measurement of the pressures in the right ventricle and pulmonary artery is also valuable because if the pressure in the right ventricle is definitely and constantly higher than that in the pulmonary artery, it is strongly suggestive of either a pulmonary stenosis or of idiopathic dilatation of the pulmonary artery.

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The oxygen consumption per liter of ventilation can also be measured in association with oximetry tests. (A Douglas bag can be used to collect the expired air and its oxygen content subsequently measured.) During exercise, a normal person will show an increase in the ratio of oxygen con-

TABLE 2.—VENOUS CATHETERIZATION STUDIES OF SOME OF THE MORE COMMON CONGENITAL CARDIAC LESIONS (AFTER BING, BURCHELL AND OTHERS).

Diagnosis	Pressures			Oxygen Content of				Possible Abnormal Locations of Catheter
	Right Auricle	Right Ventricle	Pulmonary Artery	Right Auricle	Right Ventricle	Pulmonary Artery	Peripheral Artery	
Normal	5/0	25/0	25/8	SVC = RA within 1.9 vol per cent RA = RV within 0.9 vol per cent RA = PA within 0.5 vol per cent			>RA, RV, PA	None
Auricular septal defect	moderate increase	mod inc	mod inc	>SVC	= RA	= RV	>RA, RV, PA	left auricle, pulmonary veins, left ventricle
Ventricular septal defect	normal or mod inc	normal or mod inc	normal or mod inc	normal	>RA	= RV	>RA, RV, PA	left ventricle
Eisenmenger complex	inc	inc.	inc Diastolic also inc.	normal	>RA	= RV	normal or low, but >RA, RV, PA	aorta
Tetralogy of Fallot	inc	inc	decreased	low normal	>RA	= RV	below normal but >RA, RV, PA	aorta, left ventricle?
Isolated pulmonary stenosis	inc	inc	decreased	normal	= RA	= RV	normal	none
Pulmonary stenosis with patent foramen ovale	inc	inc	decreased	normal	= RA	= RV	low but >RA, RV, PA	left auricle
Single ventricle	inc	inc	dec	low	>PA	= ventricle	low but = ventricle	?
Patent ductus arteriosus	normal, rarely inc	normal, rarely inc	normal, rarely inc.	normal	= RA	>RV	normal	aorta
Idiopathic dilatation of the pulmonary artery	normal or inc	normal or inc	decreased	normal	= RA	= RV	normal	none
Essential pulmonary hypertension	inc	inc	inc	normal	= RA	= RV	normal	none

sumed to the liters of air ventilated per minute. However, in patients who have pulmonary stenosis, the pulmonary obstruction limits the effective pulmonary blood flow and the ratio of oxygen consumed to liters of ventilation falls. If a septal defect is also present in association with the pulmonary stenosis, as in the tetralogy of Fallot, the oxygen saturation of the peripheral arterial blood will also fall.

Table 3 shows the effect of exercise on the peripheral arterial oxygen saturation, and the ratio between oxygen consumed to liters of ventilation, in some of the more common congenital cardiac lesions

Dye Dilution Curves.—A dye (indicator) dilution curve shows the changing concentration of the dye at a specific point in the vascular system at various instants following its injection at some different point in the vascular system. Usually, dilution curves of the dye are obtained from the *arterial system (by placing an oximeter on the ear) after the dye has been*

TABLE 3.—THE EFFECT OF EXERCISE ON THE OXYGEN SATURATION OF THE PERIPHERAL ARTERIAL BLOOD, AND ON OXYGEN CONSUMPTION PER LITER OF VENTILATION (AFTER BING, HANDELSMAN, CAMPBELL)

Diagnosis	*Oxygen Consumed per Liter of Pulmonary Ventilation*	*Oxygen Saturation of Peripheral Arterial Blood*
Normal	rises	unchanged
Auricular Septal Defects	rises	falls
Ventricular Septal Defects	rises	falls
Eisenmenger Complex	rises	falls
Tetralogy of Fallot	falls	falls
Isolated Pulmonary Stenosis	falls	unchanged
Patent Ductus Arteriosus	rises	unchanged

injected rapidly into the venous system proximal to the pulmonary capillaries. The dye can be injected either into the peripheral veins, or into the right heart by means of a cardiac catheter. The dye most commonly used for this purpose is Evans blue dye (T-1824). However, brilliant vital red and other dyes have been used

When the dye is injected into a peripheral vein of a normal subject, the following occurs: The oximeter responds to a decreased transmission of light, and therefore to an increased concentration of the dye in the blood stream, by a downward deflection of the recording beam After the dye is injected, there is a short interval (the appearance time) which elapses before the dye first arrives at the oximeter site. Then there is a rapid increase in concentration of the dye to a peak, followed by a less rapid decline in concentration, which is incomplete This merges into a second peak of concentration which is caused by the return of the dye to the oximeter site after it has passed the systemic capillaries and has reentered the veins

After injection into a peripheral vein, the following average normal values are found: appearance time, 14 sec. (10 to 20 sec); maximal con-

centration time, 25 sec (16 to 35 sec.); buildup time, 10 sec. (7 to 15 sec); disappearance time, 16 sec (9 to 26 sec); and recirculation time, 21 sec. (16 to 28 sec.) (Fig 61*H*)

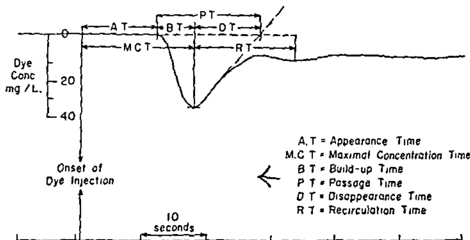


FIG 61H —A normal dye dilution curve (after Swan)

Dye dilution curves are helpful in diagnosing left-to-right and right-to-left shunts.

In a *right-to-left* shunt, as occurs in the tetralogy of Fallot, the dilution curve shows a shortened appearance time and an abnormal (first) hump on the buildup slope of the curve. This is due to the passage of a portion of the dye across the ventricular septal defect directly into the systemic circulation. The appearance time is reduced because this shunted dye reaches the oximeter before the dye which travels the longer, normal circulatory path through the lungs. As each portion of the dye is subjected to dilution in its passage through the heart and blood vessels, its arrival in the peripheral circulation takes the form of two curves which partially overlap.

The contour of the dye curve is determined mostly by the volume of blood passing through the shunt. Thus, in patients with a large right-to-left shunt, the initial abnormal deflection may be as large or larger than the normal portion of the curve

In *left-to-right* shunts, a characteristic curve also appears. The appearance time and buildup time are normal. However, the magnitude of the deflection is reduced, and the slope of declining concentration of the dye is much prolonged. Also, no peak due to systemic recirculation can be identified.

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Abnormal Venous Pressure Values

See page 114

Abnormal Vital Capacity Values

See page 115

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centration time, 25 sec. (16 to 35 sec); buildup time, 10 sec. (7 to 15 sec), disappearance time, 16 sec. (9 to 26 sec.); and recirculation time, 21 sec. (16 to 28 sec.) (Fig 61*H*).

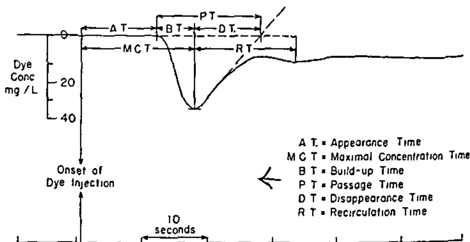


Fig 61H.—A normal dye dilution curve (after Swan)

Dye dilution curves are helpful in diagnosing left-to-right and right-to-left shunts.

In a *right-to-left* shunt, as occurs in the tetralogy of Fallot, the dilution curve shows a shortened appearance time and an abnormal (first) hump on the buildup slope of the curve. This is due to the passage of a portion of the dye across the ventricular septal defect directly into the systemic circulation. The appearance time is reduced because this shunted dye reaches the oximeter before the dye which travels the longer, normal circulatory path through the lungs As each portion of the dye is subjected to dilution in its passage through the heart and blood vessels, its arrival in the peripheral circulation takes the form of two curves which partially overlap

The contour of the dye curve is determined mostly by the volume of blood passing through the shunt Thus, in patients with a large right-to-left shunt, the initial abnormal deflection may be as large or larger than the normal portion of the curve.

In *left-to-right* shunts, a characteristic curve also appears. The appearance time and buildup time are normal. However, the magnitude of the deflection is reduced, and the slope of declining concentration of the dye is much prolonged. Also, no peak due to systemic recirculation can be identified.

Section 3. Cardiac Syndrome

INTRODUCTION

SINCE it is the function of the heart to pump out blood and thus supply the tissues with the oxygen they need, a heart can be considered normal from a physiological point of view only if it is capable of supplying the tissues with sufficient oxygenated blood for their needs Under all ordinary conditions, if the supply of oxygen to the tissues is less than the needs of the tissues, it is the heart and not the respiratory apparatus which is at fault. Thus during heavy exercise, the heart even of a normal person will fail sooner or later to deliver sufficient oxygen, and it is this defect which ultimately limits the work that a person can do However, the average normal heart is able to satisfy very heavy demands for oxygen before such a stage is reached. An abnormal heart, however, is unable to supply the tissues with sufficient oxygen on moderate work or exertion, or even at rest

From this point of view, normal or abnormal heart sounds, normal or abnormal electrocardiographic patterns, the presence or absence of murmurs, and other cardiovascular abnormalities are only of practical importance insofar as they bear directly or indirectly, in diagnosis, treatment, or prognosis, on the basic question of whether a person can or cannot carry on ordinary activity without developing symptoms or signs of cardiac distress.

In Chapter 13, which follows immediately, I shall describe the syndrome produced by the general disturbance of the heart as a pump, or congestive heart failure; in Chapter 14, page 281, the syndrome of circulatory collapse, or shock, in Chapter 15, page 287, the syndrome of syncope and related states, in Chapter 16, page 294, the anginal syndrome, in Chapter 16, page 310, the syndrome produced by psychogenic disturbances, namely the effort syndrome or neurocirculatory asthenia, and in Chapters 18, through 20, pages 316 through 360, the syndromes produced by the cardiac arrhythmias. The syndrome of pericardial tamponade is described on page 643 and the superior and inferior vena caval syndromes on pages 672 and 675

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Regardless of whether high-output or low-output failure is present, the symptoms and signs of congestive heart failure occur in three ways.

a. From inadequate blood supply to the tissues, especially the kidneys and voluntary muscles Inadequate blood supply to the voluntary muscles causes weakness and fatigue, which often are early symptoms of failure This is aggravated by exercise, because the patient in failure cannot increase his output with exercise The inadequate blood supply to the kidneys is associated with a decreased glomerular filtration and a decreased excretion of salt, resulting in retention of salt and water, increased venous pressure, and edema This mechanism has been discussed in detail on page 109, and is known as *the forward-failure theory of congestive heart failure*

b. From inability of the failing heart to empty properly, resulting in increased venous pressure and waterlogging of the tissues. Starling pointed out many years ago that the stroke volume of the heart is directly proportional to the diastolic length of the muscle fibers or to the diastolic volume of the ventricular chambers. This is known as Starling's Law Thus, if the left ventricle suddenly weakens and propels less blood than it receives from the right ventricle and lungs, there will be more blood than normal in the left ventricle at the beginning of the next systole, the diastolic volume of the left ventricle having enlarged to hold the extra blood However, because of its enlarged diastolic volume, the left ventricle is able to propel more blood at the next systole, and the heart continues to function adequately although the left ventricle has dilated Similarly, if the right ventricle suddenly fails, and the venous return continues unabated, the right ventricle will dilate in order to bring its stroke volume to its previous level

c. From electrolyte disturbances, especially a low serum sodium level (page 270). This usually occurs in patients who have been treated too vigorously with the mercurial and other diuretics

Dilatation itself is not necessarily abnormal because it has been found that in normal people the heart dilates with excessive exercise. (With moderate exercise in a normal person, Starling's Law does not hold because an increased cardiac output occurs without cardiac dilatation) If the dilatation continues for any length of time, it results in hypertrophy of the ventricle.

In addition to the dilatation of the right or left ventricle, an increased pressure occurs within the affected ventricular cavity, and in that portion of the circulatory system draining into it. This produces the characteristic clinical picture of left-sided heart failure or right-sided heart failure This mechanism of congestive heart failure is known as *the backward-failure theory of congestive heart failure*

Etiology.—A major conflict between the forward-failure theory and the backward-failure theory concerns the temporal relations between increased venous pressure and edema. According to the backward-failure theory, the failing heart causes an increased venous pressure as the first sign This produces increased capillary blood pressure and transudation of fluid from the capillaries, and a reduction of the circulating blood plasma volume. This in turn causes the kidneys to reabsorb more than the usual quantities of salt and water However, according to the forward-failure theory the

Chapter 13

CONGESTIVE HEART FAILURE

Pathological Physiology.—The signs and symptoms of congestive heart failure (cardiac decompensation, cardiac insufficiency) develop whenever the heart does not pump enough blood for a prolonged period to meet the needs of the body, or in other words, whenever the cardiac output becomes inadequate. However, there is no absolute level of cardiac output below which the signs and symptoms of failure invariably appear. For example, in a patient with rheumatic heart disease, the cardiac output at rest may be sufficient for the needs of the body, and the patient is comfortable, even though the cardiac output is below normal statistically. However, with exercise, the heart may not be able to respond to the added burden imposed by the exercise, and heart failure occurs. On the other hand, a patient with hyperthyroidism or severe anemia has a high cardiac output even at rest. When heart failure develops in such a patient, the cardiac output may fall, but it still will be higher than the output of a normal person at rest.

The reverse of this picture occurs in myxedema, where the cardiac output may be very low without any signs of failure, because the low output is adequate for the needs of the body. However, if the metabolism were increased without a corresponding increase in cardiac output, failure would occur.

The level at which the cardiac output becomes inadequate depends on the cause of the heart failure, which can be divided into three general groups:

1. **Heart Failure Due to Primary Heart Disease (Low-Output Failure).**—In this group are included failure due to acute rheumatic fever or other forms of myocarditis, rheumatic and syphilitic valvular disease, hypertensive heart disease, myocardial infarction, congenital heart disease, *etc.*

2. **Heart Failure Due Primarily to Noncardiac Disturbances (High-Output Failure).**—In this group are included failure due to hyperthyroidism (page 680), severe anemias (page 722), peripheral arteriovenous fistulas (page 663), Paget's disease (page 722), beriberi (page 711), and some cases of cor pulmonale (page 628). In all these conditions, the need for oxygen is so great that a high cardiac output results, but the energy demand on the heart is also so great that a point is reached where the heart no longer can function efficiently, and heart failure occurs. Although the cardiac output then falls, it still remains statistically higher than normal. However, the high cardiac output here is the cause of the heart failure, not the result of it.

3. In many cases, heart failure may be due to both primary and secondary factors. For example, a patient with hyperthyroidism and heart failure may also have rheumatic valvular disease or hypertensive cardiovascular disease, which itself could eventually lead to failure.

and reacts with actomyosin-ADP to reform actomyosin-ATP. The phosphocreatine, which restores the high-energy actomyosin-ATP to muscle, in turn gets its energy from the breakdown of glycogen to hexose and the breakdown of hexose to lactic acid, in a complicated series of chemical steps.

Cardiac muscle is distinguished from skeletal muscle by a relatively low phosphocreatine content Skeletal muscle has four times as much phosphocreatine as ATP, cardiac muscle has only slightly one-and-a-third times as much. This means that cardiac muscle is relatively sensitive to any interruption in the formation of phosphocreatine

One of the conditions which is able to interrupt the formation of phosphocreatine is a high intracellular sodium concentration, and it has been found that only a slight increase in the intracellular sodium level in heart muscle (and a decrease in muscle potassium) can lead to an inhibition in the formation of phosphocreatine and a decrease in the force of cardiac contraction. This disturbance is further aggravated if the extracellular potassium level is low

Thus, if heart failure is associated with a shift of intracellular electrolytes and the replacement of cellular potassium with sodium, this alone would contribute to the failure and tend to set up a vicious cycle, *viz* heart failure → increased total body fluid + entrance of sodium into the cells and a loss of cellular potassium → weakening of cardiac contractions → increasing heart failure →

Evidence for this theory can be found in observations that heart failure causes a reduction of the potassium content and an elevation of the sodium content of heart muscle, and that digitalis is able to reverse these intracellular electrolyte disturbances.

3. Hormonal disturbances —It is well known that the adrenal cortical steroids, especially the mineralocorticoids like desoxycorticosterone, can produce a retention of sodium and water even in a normal person In patients with heart failure, an increased amount of urinary corticoids and desoxycorticosterone-like material has been observed. In addition, the reduction in the sodium output in the sweat, saliva and urine of such patients has also been attributed to increased adrenocortical activity However, these observations, while suggestive, by no means prove that increased adrenocortical activity is responsible for the retention of sodium and water and for the edema of heart failure

The antidiuretic hormone, ADH, of the posterior pituitary, has also been implicated as a factor in the formation of edema because antidiuretic *material has been found in the urine of patients with heart failure and with* cirrhosis of the liver Here again, no definitive statements on the role of the posterior pituitary in either producing or maintaining edema can yet be made

Other hormones and humeral agents such as renin and VEM (vasoexciter material) have also been implicated as possible factors causing a decrease in the renal excretion of sodium and water, but their role in the formation of edema is unclear.

Precipitating Factors.—Many patients with organic heart disease go along comfortably for many years, until, gradually or suddenly, failure

increased venous pressure occurs only after the salt and water have been retained.

I believe that both theories are necessary to explain the phenomena of congestive heart failure. The forward-failure theory offers the best explanation for the production of edema, whereas the backward-failure theory explains best the varied clinical pictures of left-sided and right-sided heart failure. However, our knowledge of the physiological mechanisms of congestive heart failure is still incomplete and many phenomena still remain to be explained

So far I have been describing heart failure as a purely mechanical process Actually the problem is much more complex. For example, recent studies have indicated that heart failure is associated with the following physiological disturbances:

1. An increase in the total body water and a change in body water compartments —Total body water consists of the intracellular water content as well as the amount of extracellular water (the water in the blood and tissue spaces). It can be measured by giving the subject radioactive deuterium oxide, or tritium oxide, or by using antipyrine or some other substance which is distributed evenly throughout the water of all the tissues of the body. In discussing edema (page 126), I pointed out that it was due to an increase of extracellular fluid. However, body water measurements indicate that when edema occurs, the total body water volume increases along with an increase in extracellular water, but that there is a slight decrease in intracellular water volume. In other words, in spite of the general increase in water in a patient with edema, there is some intracellular dehydration.

2 Changes in intracellular and extracellular electrolyte levels —These changes and shifts in body water may be accompanied by shifts in electrolyte concentrations, particularly sodium and potassium, in both the cells and tissue spaces. Normally, the cells contain relatively much potassium and little sodium, and the extracellular fluids a high sodium but a low potassium concentration. In heart failure, the potassium content of the cells may decrease and the sodium concentration may rise, possibly to compensate for the loss of potassium This is one of the reasons that in chronic heart failure a low serum sodium level is found despite the fact that one of the causes of heart failure is a retention of sodium by the kidneys

According to Szent-Gyorgi, the contractile system of muscle consists of an elongated protein conjugate, *myosin*, and its precipitin, polymerized *actin*. These two proteins are attracted to each other by colloidal forces, but are kept apart by an atmosphere of potassium ions. When the muscle cell is stimulated, the cell membrane becomes permeable to cations, such as potassium. This allows potassium ions to pass out of the cell membrane. This loss of cellular potassium promotes the union of the actin and myosin to form actomyosin. These proteins then adsorb *adenosintriphosphate* (*ATP*). The resulting *actomyosin-ATP* complex becomes discharged and maximally folded, resulting in muscular contraction. As a result, the actomyosin-ATP is converted into *actomyosin-diphosphate* (*ADP*).

In order for the contracted muscle to relax and extend, the lost energy has to be restored. A new compound, *phosphocreatine*, enters the picture,

the efficient right ventricle propels more blood into the lungs than can pass into the left ventricle through the stenosed mitral valve, and pulmonary congestion occurs.

Etiology.—Acute left-sided heart failure occurs under two divergent conditions:

A. In hypertensive cardiovascular disease, coronary artery disease, and aortic valvular disease, the attacks frequently occur at night and while the patient is asleep. Such attacks are often described as *paroxysmal nocturnal dyspnea.*

Several factors produce these attacks during the early hours of sleep The patient may slide down in bed during the night, decreasing his vital capacity. In many cases, the patient states that he was awakened by a bad dream, which can produce as severe a strain on the heart as exercise. It has also been suggested that the attacks occur from overloading of the circulation as a result of resorption of edema fluid into the blood stream when the cardiac output improves during the restfulness of sleep. In addition, during the night bronchial secretions may accumulate until a paroxysm of coughing occurs This precipitates the attack by suddenly calling forth an increased output of the right and left ventricles Since the right ventricle is stronger than the left ventricle, pulmonary congestion results

B. Acute left-sided heart failure can also occur while the patient is awake, especially after severe exercise, excitement, sexual intercourse, *etc* It can also be precipitated in an apparently normal person, or in a person with only minimal cardiac weakness by the administration of excess intravenous saline, post-operatively, for example

Patients with mitral stenosis or auricular fibrillation rarely develop nocturnal dyspnea but commonly develop acute left-sided heart failure after severe exertion and other unusual circumstances, such as the burden of pregnancy. The reason the left ventricle does not fail spontaneously in such cases is that there is usually some degree of right-sided failure also present, which tends to prevent overloading of the lungs However, regardless of the cause, the clinical picture of acute left-sided failure is similar, and is due to the pulmonary congestion or actual pulmonary edema that results.

So far I have been considering purely mechanical explanations for the occurrence of acute left-sided failure and pulmonary edema. However, acute pulmonary edema can also occur in the absence of heart disease, especially with neurogenic disturbances, such as skull fractures, intracranial hemorrhage, brain tumors, even after lumbar puncture It has also appeared after the inhalation of toxic fumes and gases, after thoracic or abdominal paracentesis, *etc.*

The usual explanation for the acute pulmonary edema in such cases is that there probably occurs stimulation of the vasodilator nerves of the lungs, allowing an abnormal increase in pulmonary capillary permeability. However, recent studies of acute pulmonary edema caused by disturbances of the central nervous system, have shown that in such cases a sudden marked rise in systemic blood pressure occurs, and that it is the rise in blood pressure which produces the pulmonary edema, especially if the patient's cardiac reserve is low.

occurs. The precipitating causes of the heart failure are varied. Most often, in my experience, no one factor can be incriminated, because the onset of the failure is gradual.

Some of the more common precipitating factors are:

1. **Infections.**—An infection, even an upper respiratory infection, can precipitate heart failure by increasing the work of the heart, as a result of fever and tachycardia, or by a direct toxic effect on the myocardium.

2. **Exertion.**—Heart failure can be precipitated especially by severe exertion to which the patient is unaccustomed. In this category should be included the exertion of sports as well as of work. Sexual intercourse can also precipitate acute left-sided heart failure.

3. **Pregnancy.**—See page 749.

4. **Obesity.**—Obesity *impairs the circulation in several ways:* Because of increased intraabdominal fat, the diaphragm is elevated and the vital capacity reduced. In addition, during exercise and work, the cardiac output increases greatly because the skeletal muscles must move a large body mass.

5. **Myocardial Infarction.**—In some cases of acute myocardial infarction, the clinical picture is that of acute left-sided heart failure rather than of shock. Such patients usually have had antecedent hypertensive cardiovascular disease and some degree of chronic heart failure. Acute pulmonary embolism can also precipitate heart failure.

6. **Cardiac Arrhythmias, Especially Paroxysmal Tachycardia and Auricular Fibrillation.**—The arrhythmia results in a decreased cardiac output especially if the ventricular rate exceeds 180. However, auricular fibrillation can precipitate heart failure even when the ventricular rate is much slower. The decreased cardiac output is usually not sufficient to precipitate heart failure in a normal heart, but in the presence of even minimal hypertrophy or dilatation, it may be sufficient.

7. **Miscellaneous Factors.**—Factors, such as coughing spells, emotional upsets, acute hemorrhage, transfusions or infusions of saline (page 724), *etc.*, can also precipitate heart failure.

LEFT-SIDED HEART FAILURE

On page 230, I pointed out that the clinical picture of heart failure was due to an inadequate blood supply to the tissues and especially to the inability of the failing heart to empty properly. Inasmuch as either the function of the left or right ventricle can remain adequate while the other chamber fails, it is convenient to describe the clinical picture of heart failure in terms of left-sided and right-sided heart failure.

Acute Left-Sided Heart Failure.—Pathological Physiology.—When acute left-sided heart failure occurs, the left ventricle suddenly weakens and is unable to empty adequately during systole. Since the right ventricle still functions efficiently, more blood is pumped by the right ventricle into the lungs than can be accepted by the left ventricle, resulting in marked pulmonary congestion or acute pulmonary edema.

Acute left-sided heart failure occurs in mitral stenosis in a slightly different way. When the cardiac output suddenly increases as with exercise,

The history of the patient is often important in differential diagnosis For example, the patient with bronchial asthma gives a history of chronic cough over a period of years, the occurrence of attacks during the day as well as at night, seasonal exacerbations, relief with epinephrine; and in long-standing cases, an emphysematous chest and clubbing may be present.

At the bedside, marked distention of the neck veins may occur with either cardiac or bronchial asthma However, whereas the arm-to-tongue circulation time is prolonged in cardiac asthma, it is normal during an attack of bronchial asthma, and even after an attack of cardiac asthma the circulation time may remain prolonged. The heart and blood pressure in bronchial asthma are usually normal, whereas in cardiac asthma, enlargement of the heart is usually found on physical examination and the blood pressure is usually high. However, a patient with bronchial asthma may have coexistant hypertensive cardiovascular disease.

In doubtful cases, 0 5 gram aminophylline can be given intravenously (10 cc. ampoule) or intramuscularly (2 cc. ampoule), because it is effective in both cardiac and bronchial asthma. Epinephrine is contraindicated in cardiac asthma. Morphine is contraindicated in bronchial asthma.

Course and Prognosis.—The occurrence of acute left-sided heart failure is not a good sign, and death often follows within two years, but with proper management, the patient may live much longer. The patient may experience innumerable attacks before death finally occurs.

If the patient develops right-sided heart failure in addition to the left-sided heart failure, the attacks of acute left-sided heart failure may disappear because the weak right ventricle can no longer flood the lungs. However, when this occurs, the patient's condition is prognostically worse.

Treatment.—Several different forms of therapy are effective for acute left-sided heart failure.

A In many cases, the attack will spontaneously disappear in several hours, even without therapy. However, death though rare with an attack, may occur, and some form of active therapy should be used.

B. Therapy Directed Toward Increasing Cardiac Efficiency.—The following procedures can be used:

1. *Digitalis Preparations* —Full doses of a rapidly-acting cardiac glycoside, such as lanatoside C, (page 258), digoxin (page 258), ouabain (page 259), *etc* , can be given intravenously. I usually use lanatoside C, 6 to 8 cc (1 to 1 6 mg). Dramatic improvement is usually noted within 10 or 15 minutes.

2. *Phlebotomy* —A bloodless phlebotomy by means of tourniquets, either of rubber tubing or of blood pressure cuffs, can be applied to all four extremities, at their junction with the torso, tightly enough to obstruct the venous return, but not occluding the pulse The cuff pressure is raised to about 70 mm Hg (just below the diastolic level) and is maintained at this level for fifteen minutes The cuff pressure is then dropped to 0 mm Hg for one minute. The pressure may then be raised and the procedure repeated several times as necessary.

A much more effective procedure than tourniquets that I frequently use for decreasing the venous return is to perform a phlebotomy of approximately 500 cc. I carry in my bag a sterile $1\frac{1}{2}''$ 15 gauge needle, which can

Symptoms and Signs.—The patient is usually found sitting upright or bending forward, in intense respiratory distress, grasping the sides of the bed or chair to aid the accessory muscles of respiration by fixing the shoulder girdle. He may be cyanotic and often is covered by a cold sweat. Occasionally he will ask, gasping for air, to be moved near an open window. Productive, tickling cough is present with light, pink, frothy expectoration, due to pulmonary edema. In severe cases, the sputum literally pours out of the mouth and as much as a pint or more can be brought up in an hour or two. The patient finds that he gets some relief by letting his feet hang down from the side of the bed, thus draining some blood from the lungs into the lower extremities

Examination reveals hyperresonance of the thorax. Coarse moist râles are heard posteriorly, extending above the scapulæ, and frequently throughout the lung fields even anteriorly. Coarse tracheal gurgling râles may even be heard at a distance from the patient Occasionally, only asthmatic pipes and squeaks are present, with an expiratory type of asthmatic dyspnea (*cardiac asthma*).

There are no characteristic findings in the heart, whose sounds may be obscured by the many râles The pulmonary second sound may be accentuated and a diastolic gallop is often present. The blood pressure is markedly elevated, the systolic pressure may rise to 300 mm. or more, the diastolic pressure also rising greatly. The rise in blood pressure probably precedes the attack. A drop in blood pressure during the attack is suggestive of acute myocardial infarction. The pulse rate is usually rapid, but a slow pulse has been reported in some cases of aortic stenosis with acute left-sided failure.

Mild cases of paroxysmal nocturnal dyspnea may present few symptoms. The patient may awake with a feeling of anxiety and cough, constantly clearing his throat He may bring up some viscid sputum, feel relieved and fall asleep again in a few minutes In patients with coronary artery disease, attacks of acute left ventricular failure may occur with the symptoms of angina pectoris, especially at night.

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Electrocardiogram.—No characteristic electrocardiographic findings are present

Laboratory Tests.—The venous pressure may remain normal, because of the absence of right-sided failure. However, the marked dyspnea may cause the intrapleural pressure to become markedly positive, thus interfering with the return of the blood to the chest, and the venous pressure may rise to even 300 mm. or more of water. The arm-to-tongue circulation time may be prolonged to 2 or 3 times normal.

Diagnosis—The differentiation of cardiac asthma due to acute left-sided heart failure from bronchial asthma may be extremely difficult, because the patient may present the identical clinical picture of musical pipes and squeaks and extreme expiratory dyspnea with an absence of moist râles in either condition. However, sooner or later, a patient with cardiac asthma will develop moist basal râles if left untreated, but this is a bad sign and may usher in fatal pulmonary edema.

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long as twelve hours In such a case, the inhalation should be given for periods of three hours or less with rest periods of fifteen minutes

The only possible danger of the alcohol vapor inhalation is the hazard of ignition of the vapor. This is theoretical rather than real

The routine therapy for pulmonary edema can be given in conjunction with the alcohol vapor inhalations

Prophylaxis.—The prevention of further attacks depends on the cause of the acute left-sided failure If the patient has organic heart disease, he should be put on a regular heart-failure regimen, namely, a low-sodium diet, mercurials, digitalis, *etc* (page 247)

Chronic Left-Sided Heart Failure.—**Pathological Physiology** Chronic left-sided heart failure usually occurs in the following conditions.

A. Hypertensive Cardiovascular Disease—Patients with essential hypertension or hypertension due to chronic nephritis, *etc*, may develop left ventricular hypertrophy and dilatation and eventual left-sided failure in the following way. The hypertension with its associated increased peripheral resistance increases the work of the left ventricle and is the direct cause of the left ventricular hypertrophy Microscopic study of a hypertrophied ventricle shows that hypertrophy is not produced by an increased number of fibers, but simply by an increased thickness of the individual fibers. Since the nourishment of the fibers is obtained from the adjacent capillaries, which do not increase in number, the metabolic exchange of the hypertrophied muscle cells is impaired. This is further aggravated because the hypertrophied muscle cells require more oxygen than a normal muscle. The actual level of blood pressure is not important, and I have observed patients whose systolic pressure has been nearly 300 mm for many years without signs of heart failure

Chronic left-sided heart failure is produced in a slightly different way from acute left-sided failure With chronic fatigue of the left ventricle, due to the strain of hypertensive cardiovascular disease (or other factors producing increased work of the left ventricle), the cardiac output falls and the renal blood flow decreases, resulting in a retention of sodium and water and an increased circulating blood volume (see page 129) In addition, the failing left ventricle is unable to empty adequately during systole, and the pressure in the left ventricular cavity rises This causes a rise in left auricular pressure, which in turn causes a rise in the pressure of the pulmonary artery and in the pulmonary vessels The increased pulmonary pressure, in association with an increased volume of blood in the lungs, causes a transudation of fluid into the alveolar spaces, producing pulmonary congestion and *pulmonary edema*

B. Coronary Artery Disease—This, itself, does not cause left ventricular dilatation or failure However, when myocardial infarction occurs, left and even right-sided failure may supervene At autopsy, the scattered myocardial fibrosis which is present in such cases is evidence of the old infarction, and is not a sign of "chronic myocarditis," a term which should no longer be used

C. Aortic Valvular Lesions—Either aortic insufficiency or aortic stenosis can produce chronic left-sided heart failure.

be quickly inserted into an antecubital vein without anesthetizing the skin. The blood is allowed to spurt directly into a container or bottle. Care should be taken not to withdraw too much blood, because the patient may go into shock, in spite of the persistence of the pulmonary edema. Phlebotomy has its greatest value when the venous pressure is high.

3. *Oxygen.*—Oxygen, if available is very effective. It should be given with a mask in 100 per cent concentration. It not only alleviates the intense dyspnea but may also have some direct action on the pulmonary capillaries to decrease their permeability. It has been suggested that the 100 per cent oxygen be inhaled under positive pressure of 2 to 4 cm. of water. The increased pressure in the tracheo-bronchial tree acts as a direct physical force on the capillary walls, counterbalancing their increased hydrostatic pressure and thus decreasing the pulmonary edema. In addition, it increases the venous pressure and retards the entrance of blood into the right ventricle, thus having an action similar to tourniquets or phlebotomy.

4. *Aminophylline.*—0.5 gram ($7\frac{1}{2}$ grains) intravenously (in a 10 cc. ampoule) has been recommended because of its direct bronchial dilator action. However, it produces intense hyperpnea and I prefer not to use it in acute left-sided heart failure.

C. Therapy Directed Toward Diminishing or Abolishing Abnormal Reflexes.—Morphine, 15 mg. ($\frac{1}{4}$ grain) with or without 0.6 mg. ($\frac{1}{100}$ grain) atropine intramuscularly, is the drug of choice. The exact action of morphine is unknown. Atropine may act by drying up the bronchial secretions, but this is questionable. However, the morphine may stop the attack without additional therapy. In infants and young children, 1 mg. ($\frac{1}{60}$ grain) per 10 pounds of weight can be given intramuscularly.

D. Other Therapy.—Two new types of therapy for acute left-sided heart failure have recently been advocated:

1. Ganglionic blocking agents, such as priscoline. The drugs act as peripheral vasodilators, allowing blood to pool in the peripheral vascular bed.

2. *Alcohol Vapor Inhalation.*—Alcohol vapor has an anti-foaming action and is effective in the treatment of acute pulmonary edema. The best method of using alcohol vapor inhalation is as follows:

A nasal catheter is placed in the patient's nasopharynx in the usual manner. Oxygen is obtained from conventional equipment, consisting of a tank, adjustable pressure regulator, flowmeter and vaporizer (humidifier). Ethyl alcohol (95 per cent preferably, or 70 per cent if the higher concentration is not available) is placed in the vaporizer instead of the water which usually is contained in it. The flow of oxygen is started slowly, about 2 to 3 liters per minute, and the tubing adapter is connected to the nasal catheter. Within five to seven minutes, the oxygen flow is progressively raised to 7 or even 10 liters per minute, depending on how the patient tolerates it. This rate can then be maintained through the course of therapy.

If a mask instead of a catheter is used, 30 to 40 per cent ethyl alcohol should be used in the humidifier since higher concentrations are not well tolerated. Treatment using a tent is not effective.

The inhalation is discontinued when the pulmonary edema subsides. This may take an hour or more. Rarely, the inhalations are continued as

long as twelve hours. In such a case, the inhalation should be given for periods of three hours or less with rest periods of fifteen minutes

The only possible danger of the alcohol vapor inhalation is the hazard of ignition of the vapor This is theoretical rather than real

The routine therapy for pulmonary edema can be given in conjunction with the alcohol vapor inhalations

Prophylaxis.—The prevention of further attacks depends on the cause of the acute left-sided failure. If the patient has organic heart disease, he should be put on a regular heart-failure regimen, namely, a low-sodium diet, mercurials, digitalis, *etc* (page 247)

Chronic Left-Sided Heart Failure.—**Pathological Physiology.** Chronic left-sided heart failure usually occurs in the following conditions:

A. Hypertensive Cardiovascular Disease—Patients with essential hypertension or hypertension due to chronic nephritis, *etc*, may develop left ventricular hypertrophy and dilatation and eventual left-sided failure in the following way. The hypertension with its associated increased peripheral resistance increases the work of the left ventricle and is the direct cause of the left ventricular hypertrophy Microscopic study of a hypertrophied ventricle shows that hypertrophy is not produced by an increased number of fibers, but simply by an increased thickness of the individual fibers. Since the nourishment of the fibers is obtained from the adjacent capillaries, which do not increase in number, the metabolic exchange of the hypertrophied muscle cells is impaired This is further aggravated because the hypertrophied muscle cells require more oxygen than a normal muscle The actual level of blood pressure is not important, and I have observed patients whose systolic pressure has been nearly 300 mm for many years without signs of heart failure

Chronic left-sided heart failure is produced in a slightly different way from acute left-sided failure With chronic fatigue of the left ventricle, due to the strain of hypertensive cardiovascular disease (or other factors producing increased work of the left ventricle), the cardiac output falls and the renal blood flow decreases, resulting in a retention of sodium and water and an increased circulating blood volume (see page 129) In addition, the failing left ventricle is unable to empty adequately during systole, and the pressure in the left ventricular cavity rises This causes a rise in left auricular pressure, which in turn causes a rise in the pressure of the pulmonary artery and in the pulmonary vessels. The increased pulmonary pressure, in association with an increased volume of blood in the lungs, causes a transudation of fluid into the alveolar spaces, producing pulmonary congestion and pulmonary edema

B. Coronary Artery Disease—This, itself, does not cause left ventricular dilatation or failure However, when myocardial infarction occurs, left and even right-sided failure may supervene At autopsy, the scattered myocardial fibrosis which is present in such cases is evidence of the old infarction, and is not a sign of "chronic myocarditis," a term which should no longer be used.

C Aortic Valvular Lesions—Either aortic insufficiency or aortic stenosis can produce chronic left-sided heart failure.

be quickly inserted into an antecubital vein without anesthetizing the skin The blood is allowed to spurt directly into a container or bottle. Care should be taken not to withdraw too much blood, because the patient may go into shock, *in spite of the persistence of the pulmonary edema*. Phlebotomy has its greatest value when the venous pressure is high.

3. *Oxygen.*—Oxygen, if available is very effective It should be given with a mask in 100 per cent concentration. It not only alleviates the intense dyspnea but may also have some direct action on the pulmonary capillaries to decrease their permeability. It has been suggested that the 100 per cent oxygen be inhaled under positive pressure of 2 to 4 cm. of water. The increased pressure in the tracheo-bronchial tree acts as a direct physical force on the capillary walls, counterbalancing their increased hydrostatic pressure and thus decreasing the pulmonary edema. In addition, it increases the venous pressure and retards the entrance of blood into the right ventricle, thus having an action similar to tourniquets or phlebotomy.

4. *Aminophylline* —0 5 gram ($7\frac{1}{2}$ grains) intravenously (in a 10 cc. ampoule) has been recommended because of its direct bronchial dilator action. However, it produces intense hyperpnea and I prefer not to use it in acute left-sided heart failure.

C. Therapy Directed Toward Diminishing or Abolishing Abnormal Reflexes.—Morphine, 15 mg ($\frac{1}{4}$ grain) with or without 0 6 mg ($\frac{1}{100}$ grain) atropine intramuscularly, is the drug of choice The exact action of morphine is unknown Atropine may act by drying up the bronchial secretions, but this is questionable. However, the morphine may stop the attack without additional therapy. In infants and young children, 1 mg ($\frac{1}{60}$ grain) per 10 pounds of weight can be given intramuscularly

D. Other Therapy.—Two new types of therapy for acute left-sided heart failure have recently been advocated:

1. Ganglionic blocking agents, such as priscoline. The drugs act as peripheral vasodilators, allowing blood to pool in the peripheral vascular bed

2. *Alcohol Vapor Inhalation* —Alcohol vapor has an anti-foaming action and is effective in the treatment of acute pulmonary edema. The best method of using alcohol vapor inhalation is as follows:

A nasal catheter is placed in the patient's nasopharynx in the usual manner. Oxygen is obtained from conventional equipment, consisting of a tank, adjustable pressure regulator, flowmeter and vaporizer (humidifier) Ethyl alcohol (95 per cent preferably, or 70 per cent if the higher concentration is not available) is placed in the vaporizer instead of the water which usually is contained in it. The flow of oxygen is started slowly, about 2 to 3 liters per minute, and the tubing adapter is connected to the nasal catheter. Within five to seven minutes, the oxygen flow is progressively raised to 7 or even 10 liters per minute, depending on how the patient tolerates it. This rate can then be maintained through the course of therapy.

If a mask instead of a catheter is used, 30 to 40 per cent ethyl alcohol should be used in the humidifier since higher concentrations are not well tolerated. Treatment using a tent is not effective.

The inhalation is discontinued when the pulmonary edema subsides. *This may take an hour or more. Rarely, the inhalations are continued as*

The cut section is red or may show a rusty-brown color. Even the bronchial walls are congested and red. Microscopically, the capillaries are markedly tortuous and dilated, and encroach on the alveoli which may contain numerous red blood cells, and characteristic heart failure cells (page 151) Marked sclerosis of the small and large pulmonary arteries may be present, as well as old or recent pulmonary infarcts.

Symptoms.—Dyspnea (page 118), orthopnea (page 119), cough (page 120), hemoptysis (page 121), hoarseness (page 122), weakness and fatigue (page 123) are common symptoms

Signs.—Hyperpnea (page 151), and Cheyne-Stokes respiration (page 151) may be present. Cyanosis may also appear but it is not marked except in cases of long-standing left-sided heart failure In such cases, right-sided heart failure is usually also present. Moist basal râles, with or without pleural effusion may be present

Physical examination of the heart usually reveals signs of left ventricular enlargement (page 154). Pulsus alternans (page 142), and a diastolic gallop (page 159), may be present, and the pulmonary second sound may be accentuated (page 158)

Fever is common in patients with failure (left- or right-sided). It is due in part to the increased oxygen consumption resulting from the dyspnea of left-sided failure, and as a result of decreased heat dissipation through the skin, because with the decreased cardiac output, there is a decreased blood flow through the skin, and sweating is depressed

It has been stated that when the temperature rises more than 1° in a patient with congestive failure, it is a sign that a complication, such as pulmonary infarction, rheumatic fever, subacute bacterial endocarditis, pneumonia, *etc* is present However, I have seen several patients run an intermittent fever as high as 102° for long periods, and at autopsy only congestive changes were present.

Fluoroscopic and X-Ray Examination—Signs of pulmonary congestion (page 194) are present Pleural effusion may also be present, more marked on the right side than on the left side (page 169) There may also be effusion into the interlobar fissures

Electrocardiogram.—There are no electrocardiographic signs which indicate chronic left-sided (or right-sided) heart failure However, in cases of long-standing failure, the tracing may show signs of left or right ventricular hypertrophy or strain, or both, abnormal T waves; right or left bundle branch block; old myocardial infarction, arrhythmias, especially auricular fibrillation, *etc.* However, all these electrocardiographic signs may occur without heart failure.

Laboratory Tests.—The vital capacity is markedly decreased and may be 1 liter or less. Venous pressure is normal, as is arm-to-lung circulation time However, arm-to-tongue circulation time is moderately or markedly prolonged (page 221).

Blood lactic acid levels may be elevated to as much as 100 mg. per cent (Normally, there is less than 25 mg. per cent in the resting state.) And with moderate exercise, the level rises still higher, unlike in health where the rise after moderate exercise is minimal

Aortic Insufficiency.—Aortic insufficiency usually occurs in rheumatic heart disease and in syphilitic heart disease. Cardiac hypertrophy results because the regurgitating blood increases the diastolic volume of the left ventricle and causes it to perform more work. Experiments in dogs have shown that left ventricular hypertrophy can occur within a week after the aortic valve is made incompetent. Functional aortic insufficiency usually is transient but also increases the work of the heart.

The volume of regurgitation is much greater in syphilitic aortic insufficiency than in rheumatic aortic insufficiency, because pure insufficiency occurs with syphilis whereas some degree of aortic stenosis is usually present in the rheumatic cases. Therefore the left ventricle in a patient with syphilitic aortic insufficiency is much larger than in a patient with rheumatic aortic insufficiency. However, regardless of the etiology of the aortic insufficiency, heart failure may be absent for many years.

Aortic Stenosis.—Because of the decrease in the size of the valve orifice, greater resistance is offered to the expulsion of blood from the left ventricle, and hypertrophy eventually occurs. In cases of congenital subaortic stenosis, the hypertrophy may be minimal. If the stenosis were so marked that hardly any blood could be expelled, left ventricular hypertrophy would not occur.

D. Mitral Valvular Lesions.—Mitral insufficiency or mitral stenosis can produce chronic left-sided heart failure.

Mitral Insufficiency.—When mitral insufficiency, functional or organic, occurs, the regurgitating blood enters the left auricle during systole. During diastole, this extra blood is emptied into the left ventricle, which dilates to increase its stroke volume. The actual increase in the work of the left ventricle therefore depends on the amount of regurgitating blood.

Mitral Stenosis.—In the early stages, the flow of blood from the left auricle to the left ventricle is impeded because of the mitral stenosis. The pressure in the left auricle rises, and left auricular dilatation and hypertrophy occur. Eventually the increased left auricular pressure is transmitted to the pulmonary veins and the pulmonary vessels, producing the clinical picture of left-sided heart failure. In such cases, the left ventricle is not hypertrophied, unless mitral insufficiency is also present, and if the mitral stenosis is very marked, atrophy of the left ventricle may occur because expulsion of the small amount of blood it receives from the left auricle entails very little work.

The engorgement of the pulmonary circulation in cases of mitral stenosis eventually becomes so marked that it extends to the pulmonary artery. Then the right ventricle must work against a high pulmonary arterial resistance, resulting in right ventricular dilatation, hypertrophy and eventual right-sided failure as the final phase of mitral stenosis.

E. Other Conditions.—Hyperthyroidism, severe anemias, arteriovenous fistulas and other conditions with a high cardiac output usually produce signs of both left- and right-sided heart failure.

Pathology.—Because of the intense pulmonary congestion, the lungs do not collapse at autopsy when the chest is opened. They are soggy, and when cut, show less crepitation than normal due to the decreased aeration.

The cut section is red or may show a rusty-brown color. Even the bronchial walls are congested and red. Microscopically, the capillaries are markedly tortuous and dilated, and encroach on the alveoli which may contain numerous red blood cells, and characteristic heart failure cells (page 151) Marked sclerosis of the small and large pulmonary arteries may be present, as well as old or recent pulmonary infarcts

Symptoms.—Dyspnea (page 118), orthopnea (page 119), cough (page 120), hemoptysis (page 121), hoarseness (page 122), weakness and fatigue (page 123) are common symptoms

Signs.—Hyperpnea (page 151), and Cheyne-Stokes respiration (page 151) may be present. Cyanosis may also appear but it is not marked except in cases of long-standing left-sided heart failure In such cases, right-sided heart failure is usually also present Moist basal râles, with or without pleural effusion may be present

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Laboratory Tests.—The vital capacity is markedly decreased and may be 1 liter or less. Venous pressure is normal, as is arm-to-lung circulation time However, arm-to-tongue circulation time is moderately or markedly prolonged (page 221)

Blood lactic acid levels may be elevated to as much as 100 mg. per cent (Normally, there is less than 25 mg per cent in the resting state.) And with moderate exercise, the level rises still higher, unlike in health where the rise after moderate exercise is minimal

The elevated lactic acid level is due to skeletal muscle anoxemia, resulting from the pulmonary congestion. (In patients with right-sided failure, high lactic acid levels also occur. Here it is due to anoxemia resulting from stagnation of blood. In addition, the congested liver is not able to destroy the lactic acid in normal quantities)

Basal Metabolism.—The basal metabolic rate may be elevated to + 60. This is due to the pulmonary congestion which greatly increases the work of the respiratory muscles. In addition, a greatly hypertrophied and dilated heart uses much more oxygen than a normal heart. Fever, if present, also raises the metabolic rate.

The metabolic rate may also be elevated in cases of right-sided failure if the cardiac output is high due to anemia, *etc.* However, in the usual case of right-sided failure with a low cardiac output, the metabolic rate will be normal, unless dyspnea is present

Diagnosis.—The dyspnea of obese persons, and the sighing dyspnea of neurotic individuals (page 119) should not be mistaken for the dyspnea and orthopnea of chronic left-sided heart failure. Similarly, the appearance of basal crepitant râles which occur normally due to the expansion of small patches of unaerated lung should not be confused with the moist râles of left-sided failure.

Chronic pulmonary disease may result in dyspnea, cough and even cyanosis, but in such cases, the circulation time is normal and the heart not enlarged unless cor pulmonale has resulted

Course and Prognosis.—The course and prognosis of either chronic left-sided or right-sided heart failure is similar and is described on page 247.

Treatment—The treatment of chronic left-sided and right-sided heart failure is also similar and is described on page 247.

RIGHT-SIDED HEART FAILURE

Acute Right-Sided Heart Failure.—**Pathological Physiology.**—When acute right-sided heart failure occurs in a person previously healthy, as after massive pulmonary infarction, the clinical picture is that of shock rather than of heart failure In most cases of acute right-sided failure, there has been sufficient previous weakening of the heart to make the cardiac output inadequate for the needs of the body Thus the renal blood flow is decreased, and a retention of sodium and water has occurred. With the onset of the acute right-sided failure, the weakened right ventricle is not able to expel the blood brought to it, and a marked increase in venous pressure occurs, the liver becomes engorged, and peripheral edema appears (page 129). The sudden dilatation of the right ventricle may also produce functional tricuspid insufficiency

Etiology.—Acute right-sided heart failure occurs in those conditions which produce chronic right-sided failure (page 244). It is often found when heart failure occurs during the course of acute rheumatic fever or any infectious myocarditis, or when heart failure occurs because of severe anemias, or beriberi.

Symptoms.—Intense right upper abdominal pain, due to stretching of the ...nded liver capsule, may simulate a gall bladder colic or acute chole...ystitis. Dyspnea or orthopnea is not present.

Signs.—Cyanosis is often present. It is peripheral in type, due to stagnation of blood (page 133). The neck veins are markedly distended, and may show inspiratory filling, or systolic pulsation even though tricuspid insufficiency is not present (see page 148). The liver is enlarged and may extend to below the umbilicus It is tender on palpation. A positive hepato-jugular reflux is present (page 110) The intense congestion of the liver may result in jaundice (page 135). Peripheral edema is present.

Functional Tricuspid Insufficiency —Functional tricuspid insufficiency may occur, with the following signs. The blood regurgitates from the right ventricle into the right auricle, the superior and inferior vena cavæ and the liver Therefore a characteristic systolic pulsation of the liver appears (page 172) However, the absence of liver pulsation does not rule out tricuspid insufficiency. Marked systolic pulsation of the jugular veins may also be present (page 149). The pulsations may even be noted on the dorsal veins of the hand Systolic retraction of the chest wall near the sternum may occur, due to the rapid fall in intrathoracic pressure, resulting from the large quantity of blood entering the liver during systole A systolic murmur near the xiphoid process may appear, due to the impact of the regurgitating blood on the tricuspid valve, but it is unimportant, and is more often absent than present (see page 165).

Fluoroscopic and X-Ray Examination.—There may appear to be generalized enlargement of the cardiac shadow The right auricular contour is prominent, and the superior vena cava is well visualized (page 192)

Electrocardiogram —No characteristic findings are present, but acute right ventricular strain may develop (page 211)

Laboratory Tests —See page 246

Diagnosis.—The clinical picture of acute right-sided heart failure is easy to recognize However, the sudden distention of the liver capsule may produce intense right upper abdominal pain, muscular rigidity, vomiting and even fever, which may simulate an acute cholecystitis

Treatment.—The treatment is the same as for chronic right-sided heart failure, page 247

Chronic Right-Sided Heart Failure.—Pathological Physiology and Pathology.—When chronic right-sided heart failure occurs, the congestion of the systemic veins may cause marked alterations in the kidneys, the liver and spleen, the central nervous system and in other organ systems.

The Effect of Chronic Right-Sided Heart Failure on the Kidneys —One of the earliest manifestations of either right- or left-sided heart failure is a decreased cardiac output, either absolute or relative, and a marked decrease in renal blood flow, resulting in a decrease in the volume of urine formed However, in cases of chronic right-sided failure, pathological changes in the kidneys and urine may occur At autopsy, the kidneys are found enlarged and with venous engorgement The glomeruli are not greatly affected, but cloudy swelling and other changes may appear, especially in the cells of the proximal convoluted tubules.

The Effect of Chronic Right-Sided Heart Failure on the Liver, Spleen and Gastrointestinal Tract —With prolonged right-sided heart failure the liver is markedly engorged and may show pathological changes described on page 173.

The elevated lactic acid level is due to skeletal muscle anoxemia, resulting from the pulmonary congestion (In patients with right-sided failure, high lactic acid levels also occur. Here it is due to anoxemia resulting from stagnation of blood In addition, the congested liver is not able to destroy the lactic acid in normal quantities.)

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The metabolic rate may also be elevated in cases of right-sided failure if the cardiac output is high due to anemia, *etc.* However, in the usual case of right-sided failure with a low cardiac output, the metabolic rate will be normal, unless dyspnea is present

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Etiology.—Acute right-sided heart failure occurs in those conditions which produce chronic right-sided failure (page 244). It is often found when heart failure occurs during the course of acute rheumatic fever or any infectious myocarditis, or when heart failure occurs because of severe anemias, or beriberi.

Symptoms.—Intense right upper abdominal pain, due to stretching of the distended liver capsule, may simulate a gall bladder colic or acute cholecystitis. Dyspnea or orthopnea is not present.

Signs.—Cyanosis is often present. It is peripheral in type, due to stagnation of blood (page 133). The neck veins are markedly distended, and may show inspiratory filling, or systolic pulsation even though tricuspid insufficiency is not present (see page 148). The liver is enlarged and may extend to below the umbilicus It is tender on palpation. A positive hepatojugular reflux is present (page 110) The intense congestion of the liver may result in jaundice (page 135). Peripheral edema is present.

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Fluoroscopic and X-Ray Examination.—There may appear to be generalized enlargement of the cardiac shadow The right auricular contour is prominent, and the superior vena cava is well visualized (page 192).

Electrocardiogram.—No characteristic findings are present, but acute right ventricular strain may develop (page 211).

Laboratory Tests.—See page 246

Diagnosis—The clinical picture of acute right-sided heart failure is easy to recognize. However, the sudden distention of the liver capsule may produce intense right upper abdominal pain, muscular rigidity, vomiting and even fever, which may simulate an acute cholecystitis.

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The Effect of Chronic Right-Sided Heart Failure on the Liver, Spleen and Gastrointestinal Tract.—With prolonged right-sided heart failure the liver is markedly engorged and may show pathological changes described on page 173.

The spleen may be enlarged or even atrophic. The remainder of the gastrointestinal tract shows only slight mucosal congestion even though severe right-sided failure may be present

The Effect of Chronic Right-Sided Failure on the Central Nervous System.—At autopsy, marked venous congestion of the brain is present. The leptomeninges are thickened and edematous, and the substance of the brain may be softened as a result of edema, with histological changes in the ganglion cells and in other nervous elements Because of the increased venous pressure, the pressure of the cerebrospinal fluid can be markedly increased, even exceeding 300 or more mm of water However, neurological signs of increased pressure or papilledema do not appear

Etiology.—Chronic right-sided heart failure may occur in the following conditions

1. *Chronic Pulmonary Disease*—Here the resultant obstruction to the flow of blood through the lungs causes right ventricular dilatation, hypertrophy, and eventual failure. This is discussed in detail in Chapter 40, page 626

2 *Congenital Heart Disease.*—In congenital lesions producing pulmonary stenosis or septal defects with a left-to-right shunt, right ventricular dilatation, hypertrophy, and eventual failure will also occur.

3 *Chronic Left-Sided Heart Failure.*—Chronic right-sided heart failure frequently occurs as a late stage in patients who have chronic left-sided failure. In such cases, the left-sided failure produces pulmonary congestion and hypertension of the pulmonary circulation, which results in right ventricular dilatation, hypertrophy, and eventual failure.

There is another mechanism by which right-sided heart failure can occur in patients who have massive left ventricular hypertrophy. In such patients, concentric hypertrophy of the left ventricle may cause the interventricular septum to bulge into the right ventricular cavity so much that incomplete filling of the right ventricle occurs, producing the clinical picture of right-sided failure, in the absence of signs of left-sided failure. This is known as Bernheim's syndrome.

4 *Chronic Constrictive Pericarditis.*—Here, the inflammatory fusion of the parietal and visceral layers of pericardium and the resultant scar formation prevent the ventricles from expanding during diastole to receive adequate blood. As a result the heart remains small, but intense engorgement of the systemic venous system occurs, with marked enlargement of the liver and massive, recurrent ascites. Subcutaneous edema of the lower extremities may not be present in spite of the large liver and the ascites. This is difficult to explain because ascites without edema of the lower extremities occurs with cirrhosis of the liver rather than with heart failure, but in cases of chronic constrictive pericarditis, the liver does not show cirrhotic changes. However, scar formation may involve the hepatic veins where they open into the inferior vena cava, just above the diaphragm. This would produce a marked localized increase in the venous pressure of the liver, resulting in ascites.

Left-sided failure is usually absent in chronic constrictive pericarditis, because the little blood that is pumped into the lungs by the right ventricle can be handled adequately by the left ventricle However, if pericardial

adhesions form around the pulmonary veins or the left auricle, interfering with the return of blood to the left ventricle, marked pulmonary congestion may occur

5 *Other Conditions* —Chronic right-sided and left-sided heart failure may occur simultaneously in conditions which impair the efficiency of both the right and left sides of the heart, as in rheumatic heart disease with combined mitral and aortic lesions, hyperthyroidism, severe anemias, *etc.*

Symptoms.—General symptoms of weakness and fatigue may be present. Complaints, such as anorexia, nausea, even vomiting, distention and belching, are common. The exact cause of these symptoms is obscure, because gastric function remains normal. They may be produced by the engorged liver, which also may cause a chronic nagging pain in the right upper quadrant

Numerous complaints of central nervous system origin may appear These may be minor and include forgetfulness, inability to concentrate, *etc.* However, cases of syncope, convulsions and even coma as a result of acute heart failure have been reported Such symptoms may result from a sudden decrease in cardiac output, with failure resulting in a shock-like state

A very common central nervous system effect of failure is insomnia and intense restlessness at night, the patient at times becoming disoriented or suffering hallucinations and delusions of persecution (by relatives, the physician, the nurse, *etc.*) I have seen this particularly in elderly patients in failure, who also probably suffered from cerebral arteriosclerosis The ordinary sedatives and hypnotics have no value here, but oxygen, and aminophylline (parenterally or rectally) are of value. Mental symptoms can also occur in elderly patients after excess mercurial diuresis. In such cases, the symptoms are due to excess dehydration

Nycturia (page 123) is a common symptom because of poor renal function In addition, there is oliguria and decreased sweating

Signs.—The clinical picture of chronic right-sided heart failure is due to the deficient cardiac output and to the venous engorgement of the systemic veins The neck veins are distended, may show systolic pulsation (page 149) or inspiratory filling (page 148) The engorged liver may extend to the umbilicus or below it On palpation it may be tender The liver edge may be firm, especially if liver congestion has been present for any length of time A positive hepato-jugular reflux (page 110) is present. Ascites,(page 172) and even splenomegaly may appear, as well as pleural effusion (page 169) Edema (page 126) may be extensive, and anasarca may be present. Cyanosis, due to venous stasis may develop (page 133) Jaundice (page 135) may also appear.

Examination of the heart may reveal few abnormal signs. There is usually a sinus tachycardia or auricular fibrillation The area of cardiac dullness may extend to the right of the sternum (page 156) A diastolic gallop (page 159) may appear.

Fluoroscopic and X-Ray Examination.—Generalized enlargement of the heart may be present (page 182). The superior vena cava and right auricle are prominent. The lung fields remain clear.

Electrocardiogram.—No characteristic findings are present.

The spleen may be enlarged or even atrophic. The remainder of the gastrointestinal tract shows only slight mucosal congestion even though severe right-sided failure may be present

The Effect of Chronic Right-Sided Failure on the Central Nervous System. —At autopsy, marked venous congestion of the brain is present. The leptomeninges are thickened and edematous, and the substance of the brain may be softened as a result of edema, with histological changes in the ganglion cells and in other nervous elements. Because of the increased venous pressure, the pressure of the cerebrospinal fluid can be markedly increased, even exceeding 300 or more mm of water. However, neurological signs of increased pressure or papilledema do not appear

Etiology.—Chronic right-sided heart failure may occur in the following conditions.

1 *Chronic Pulmonary Disease.*—Here the resultant obstruction to the flow of blood through the lungs causes right ventricular dilatation, hypertrophy, and eventual failure This is discussed in detail in Chapter 40, page 626

2 *Congenital Heart Disease.*—In congenital lesions producing pulmonary stenosis or septal defects with a left-to-right shunt, right ventricular dilatation, hypertrophy, and eventual failure will also occur.

3. *Chronic Left-Sided Heart Failure.*—Chronic right-sided heart failure frequently occurs as a late stage in patients who have chronic left-sided failure In such cases, the left-sided failure produces pulmonary congestion and hypertension of the pulmonary circulation, which results in right ventricular dilatation, hypertrophy, and eventual failure.

There is another mechanism by which right-sided heart failure can occur in patients who have massive left ventricular hypertrophy. In such patients, concentric hypertrophy of the left ventricle may cause the interventricular septum to bulge into the right ventricular cavity so much that incomplete filling of the right ventricle occurs, producing the clinical picture of right-sided failure, in the absence of signs of left-sided failure. This is known as Bernheim's syndrome.

4. *Chronic Constrictive Pericarditis* —Here, the inflammatory fusion of the parietal and visceral layers of pericardium and the resultant scar formation prevent the ventricles from expanding during diastole to receive adequate blood. As a result the heart remains small, but intense engorgement of the systemic venous system occurs, with marked enlargement of the liver and massive, recurrent ascites. Subcutaneous edema of the lower extremities may not be present in spite of the large liver and the ascites This is difficult to explain because ascites without edema of the lower extremities occurs with cirrhosis of the liver rather than with heart failure, but in cases of chronic constrictive pericarditis, the liver does not show cirrhotic changes However, scar formation may involve the hepatic veins where they open into the inferior vena cava, just above the diaphragm This would produce a marked localized increase in the venous pressure of the liver, resulting in ascites.

Left-sided failure is usually absent in chronic constrictive pericarditis, because the little blood that is pumped into the lungs by the right ventricle can be handled adequately by the left ventricle. However, if pericardial

Course and Prognosis.—The course and prognosis of congestive heart failure has improved markedly in recent years, due in large measure, to the use of mercurial diuretics and to the low-sodium diets, and the old observation that once venous congestion appeared, the duration of life was only two and a half years, no longer holds. Frequently death is due to a complication, such as pulmonary or systemic infarction, or intercurrent infection.

An important factor in determining prognosis is the etiology of the heart failure. Heart failure due to a condition, such as anemia, which is amenable to treatment often has a good prognosis, whereas, if the failure is due to chronic, progressive pulmonary disease, or rheumatic mitral stenosis, which is progressive, the outlook is poor.

THE TREATMENT OF CONGESTIVE HEART FAILURE

Guides to the Effectiveness of Therapy.—One of the most important guides to therapy is the weight of the patient. The patient in failure who improves, loses weight Conversely, a sudden gain in weight frequently occurs even before edema and other objective signs of failure appear.

When therapy is started, an attempt should be made to remove as much excess fluid as possible, bringing the patient's weight to a level where the optimum amount of extracellular fluid remains in the body. This has been called the "dry weight" However, excess removal of extracellular fluid is not only not beneficial but may be harmful, and can produce symptoms of dehydration, such as increased weakness, muscular cramps, even mental symptoms, coma, a sudden rise in temperature, *etc.* (salt depletion syndrome—page 270)

The weight of the patient can also be used to determine how often he should receive therapy, such as a mercurial injection. For example, if after the injection, the patient loses 2 or 3 pounds, and it takes three days for fluid to reaccumulate and for his weight to return to the original level, an injection twice a week is indicated. Even when the patient no longer requires therapy, he should weigh himself weekly. A gain in weight over a long period, however, does not necessarily indicate the return of failure but may be a sign of improved nutrition and better eating habits.

For bed-ridden patients, the specific gravity of the urine can be used as a measure of the effectiveness of therapy, because with failure, it is very high, and falls with diuresis Another test that can be used for patients with left-sided failure is the vital capacity, which rises as pulmonary congestion diminishes. The decrease in the ventricular rate to about 70 is a good sign in patients who have auricular fibrillation. However, if the patient is taking digitalis, a further decrease to 60 or less may occur, not because of improvement, but because of the development of toxic *a–v* block.

Other objective signs of improvement are the disappearance of subcutaneous edema, decrease in the size of the liver, loss of a positive hepatojugular reflux, and improvement in the general appearance of the patient.

Methods of Treatment.—The treatment of congestive heart failure is based on the following· (1) restriction of activity, (2) low-sodium diet; (3) diuretics, especially the mercurials; and (4) digitalis

Laboratory Tests.—The venous pressure is usually more than 150 mm. of water. Arm-to-lung circulation time is usually prolonged beyond nine seconds However, if high-output failure is present, the arm-to-lung circulation time may be normal The arm-to-tongue circulation time usually remains within normal even though the arm-to-lung time is prolonged. The vital capacity may be reduced, due to generalized weakness.

Blood nonprotein nitrogen and urea values are at a high normal level, but the nonprotein nitrogen can rise as high as 100 mg. per cent, or more, when the failure is severe Because of the hepatic congestion, abnormal liver function test findings are common (page 136).

The sedimentation rate is often elevated in congestive heart failure. The reason for this is unknown.

The urine is dark-brown, due to increased urobilinogen (resulting from impaired liver function). The volume may only be 400 or 500 cc. daily. Its specific gravity is usually above 1.020 and may reach 1 035. However, if right-sided failure occurs in the course of chronic glomerular nephritis, the specific gravity of the urine may remain low. Albumin, even in large amounts, may be present, as well as red blood cells, white blood cells, hyaline and even granular casts. The concentration of uric acid and urates is greatly increased, so that when the urine stands, a marked yellowish-red uric acid sediment may settle out. The chloride content of the urine is very low, and with very severe failure may be almost undetectable. With diuresis, the specific gravity of the urine falls, the color lightens, and the abnormal constituents gradually disappear

The low plasma protein level often seen in severe right-sided heart failure is probably due to malnutrition rather than to loss of protein through the urine.

Diagnosis—Cirrhosis of the liver can produce ascites, edema of the lower extremities and pleural effusion and thus can simulate chronic right-sided heart failure However, from the patient's history, one can elicit the fact that the ascites preceded the edema, whereas in chronic heart failure, the edema precedes the ascites. In addition, in cirrhosis, the venous pressure of the upper extremities is normal, circulation time test values are normal, and the hepato-jugular reflux is negative. A similar situation holds for other abdominal conditions that produce ascites and edema.

The differentiation of the nephrotic syndrome from right-sided heart failure is usually not difficult because the heart is not involved in nephrosis, whereas dilatation of the heart or signs of valvular heart disease are present in right-sided failure. Marked urinary abnormalities occur in both conditions but fat cells, which appear in the nephrotic syndrome are not present in right-sided failure.

Chronic constrictive pericarditis is often mistakenly treated for chronic right-sided heart failure for many years. However, in constrictive pericarditis, the heart is usually though not necessarily small, the electrocardiogram shows characteristic *T* wave changes, and calcification is often present in the pericardium.

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7. Sweets such as sugar, honey, molasses, jellies, jams, marmalade or preserves which do not contain sodium benzoate
8. Desserts such as jello, custards, junkets and puddings prepared with the milk allowance and no added salt
9. Frozen foods in general can be used However, frozen peas and lima beans are usually salted during the processing stage In addition, frozen fish fillets are also prepared with salt.

The following are forbidden:
1. Salt.
2 Delicatessen products, and all smoked or brine-cured and salted foods, such as ham, bacon, pickles, relishes, smoked fish, potato chips, popcorn, salted nuts, many candies, etc.
3. Bread and bread products, unless specially baked without salt.
4. Milk —Whole milk contains about 1.5 grams of salt per quart and thus should not be used in a low-sodium diet However, *lonalac*, a specially prepared salt-poor milk powder, can be used in its stead Unsalted butter can also be used
5. Cheeses, salt-butter, and margarine
6. Canned and packaged foods which contain salt. The patient should be instructed to read the labels of all canned and packaged food
7 Sodium-containing products and medications, such as self-rising flours and cake-mixes, bicarbonate of soda, baking soda, Alka-seltzer, Tums, salt gargles and tooth pastes containing sodium, laxatives containing sodium salts, carbonated drinks, etc.

The degree to which the patient follows a low-sodium diet can be checked by determining the urinary excretion of chloride in the following way. To 10 drops of urine in a test tube, add 1 drop of 10 per cent potassium chromate solution. Then a 0.73 per cent solution of silver nitrate (kept in a dark bottle to protect it from light) is added, drop by drop and the mixture shaken between drops, until a permanent light brown or brick red color appears. Each drop of silver nitrate represents the equivalent of 0 25 gram of sodium chloride per liter of urine.

The test should be done on a fasting morning specimen of urine If the patient is adhering to the diet, the urine should contain not more than the equivalent of 1.5 grams of sodium chloride per liter If the patient has been taking chloride in the form of medication such as ammonium chloride, *etc.*, abnormally high values will be obtained On the other hand, if the patient consumes sodium in the forms of salts other than chloride (such as bicarbonate, *etc.*) the test will not detect this.

The low-sodium diet is not without danger if used over a long period of time. Marked weakness may occur. Also, in patients with chronic renal disease, the renal blood flow may decrease so much that uremia may result

During an acute exacerbation of heart failure, the patient often does well on a semi-liquid, low-sodium diet consisting of milk, fruits and fruit juices, or on the original Karell diet which consists of 250 cc milk every six hours Then, in a few days, the regular low-sodium diet can be started.

The rigid low-sodium diet is difficult for the patient to follow, especially after he becomes ambulatory and returns to work, because meats and vegetables are salted in restaurants However, a patient who has been in failure should continue on a salt-poor diet indefinitely.

Other Dietary Measures.—Many patients in failure are also obese, which imposes an additional burden on the heart. I therefore routinely place my ambulatory cardiac patients on a low-caloric diet of approximately 800

1. **Restriction of Activity.**—Restriction of activity is valuable in the treatment of congestive heart failure, but rest in bed is dangerous. The reason for this is that even with a comparatively short rest period of two weeks, the danger of phlebothrombosis and thrombophlebitis of the lower extremities and pulmonary embolism is great, and many a patient in failure, whose progress has been interrupted by a sudden exacerbation of dyspnea, cough, and a rise in temperature (due to unrecognized small pulmonary infarcts) has been erroneously thought to have had a relapse, and has been mistreated by continued bed-rest The result is frequently continued embolization and even death

This, of course, does not deny the tremendous value of rest, especially in the acute stages of failure. For example, it has been pointed out that the resting oxygen consumption of the body per minute is only about 300 cc. compared to a consumption of as much as 1800 cc. per minute, during exercise. The bed rest need not be absolute, and bathroom privileges should be allowed. However, many patients are glad to get a few day's complete rest in bed. But every effort should be made to make the patient ambulatory as quickly as possible, using a low-sodium diet, rapid digitalization, oxygen even if the patient is not cyanotic, mercurial or other diuretics, thoracentesis or paracentesis if necessary.

The patient should be allowed to, and encouraged to return to work as soon as the overt signs of failure regress and the feeling of weakness disappears. If possible, he should be advised against heavy manual work, and excess stair-climbing, which is very strenuous. Many patients who are unable to do a full day's work, are quite comfortable working part-time.

2. **Salt-Poor and Low-Sodium Diets** (see also pages 562 and 563) —The importance of salt-poor and low-sodium diets in the treatment of congestive failure cannot be overemphasized, because, as was pointed out on page 109, retention of salt and water is one of the major factors in the development of edema and other signs of failure The low-sodium diet is more than just a salt-poor diet For example, the average diet contains 6 to 15 grams of salt (NaCl) a day *When salt is omitted from the table in a salt-poor* diet, the level in the diet drops to 4 to 7 grams, when salt is also omitted from the cooking, 3 to 4 grams, whereas a low-sodium diet contains only about 400 to 600 mg sodium (1 to 1.5 grams salt) a day.

Low-Sodium Diet

The following foods are allowed:

1. Meat, fresh-water fish, or poultry prepared and served without salt. Jewish women should be instructed not to "kosher" the foods One or two eggs can be eaten daily

2. All vegetables except beets, kale, celery and spinach, prepared and served without salt.

3. All fruits.

4 Cooked cereals, such as oatmeal, instant ralston, cream of wheat, farina, etc. Shredded wheat and spaghetti are also low in sodium.

5. Flavors and condiments such as allspice, caraway, chocolate (not candy), cinnamon, cocoa, curry powder, dill, garlic, ginger, lemon extract, mace, mustard powder (not prepared mustard), nutmeg, onion powder, parsley, pepper, sage, sugar, *thyme, tumeric, vanilla extract, vinegar, etc.*

6 Beverages such as coffee, tea, *fruit* juices, and water *ad lib., unless the local* water supply has a high sodium content of more than 3 mg. per hundred cubic centimeters, or unless the water has been treated in water-softening equipment.

7. Sweets such as sugar, honey, molasses, jellies, jams, marmalade or preserves *which do not contain sodium benzoate*
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The rigid low-sodium diet is difficult for the patient to follow, especially after he becomes ambulatory and returns to work, because meats and vegetables are salted in restaurants However, a patient who has been in failure should continue on a salt-poor diet indefinitely.

Other Dietary Measures.—Many patients in failure are also obese, which imposes an additional burden on the heart. I therefore routinely place my ambulatory cardiac patients on a low-caloric diet of approximately 800

calories (not necessarily a low-sodium diet), and have found that a weight loss of 1 to 1½ pounds a week can be accomplished without too much effort. To curb the appetite, benzedrine, 5 to 10 mg. can be given after breakfast and lunch I have found the following low-caloric diet satisfactory:

Low-Caloric Diet

Breakfast

1 small orange
1 egg (soft-boiled, hard-boiled or poached)
cup of coffee with skim milk, no sugar
¾ cup of cereal such as oatmeal, farina, etc.

Lunch

serving of meat, 3" × 2" × ½", with one slice of bread
glass of milk
small serving of fruit

Supper

serving of meat, fish or chicken, 3" × 2" × ½" (2 ounces)
a cupful of vegetables
small serving of fruit

Food to be avoided

salt, salted foods, butter, mayonnaise, salad dressing, gravy, fried food, cake, candy, ice cream

If the patient finds the above diet weakening, additional vegetables can be allowed Regardless of the type of diet the patient is following, he is instructed always to leave the table feeling a little hungry.

3 **The Mercurial Diuretics.**—The most effective diuretics are the organic mercury compounds which act by reducing the ability of the distal renal tubules to reabsorb sodium chloride and water. The loss of sodium and water through the urine decreases the circulating blood volume and thus decreases the venous pressure and the congestion of the viscera. Diuresis starts in about one or two hours and lasts twelve to twenty-four hours In this period about 85 per cent of the injected mercury is excreted in the urine

The specific site of the action of the mercurials is in the distal, ascending limb of Henle's loop. The mercurials decrease the retention of sodium by inhibiting the succinic dehydrogenase enzyme system in Henle's loop.

Indications for the Use of the Mercurial Diuretics.—The mercurial diuretics are effective in both chronic right-sided and left-sided heart failure. In the treatment of acute right- or left-sided failure they can also be used, but one should remember that it takes at least an hour for the diuretic action to start, whereas rapid digitalization, or phlebotomy, or oxygen, or morphine, act much more promptly.

The mercurials have been used prophylactically and diagnostically in patients whose symptoms are suggestive of early left-sided heart failure because after an injection, the patient may lose several pounds in weight, his respiratory distress may disappear, and the vital capacity may rise. However, even a normal person may experience a marked diuresis and loss of weight after a mercurial.

Shall Mercurial Diuretics Be Used in All Cases of Heart Failure?—The patient in mild heart failure often responds to a low-sodium diet, and a low-

caloric diet, if obesity is also present. However, if this does not alleviate symptoms, the mercurials should be used in conjunction with digitalis preparations.

Mercurial Preparations and Dosage.—The mercurial preparations in common use are mercuhydrin (meralluride), mercuzanthin (mercurophylline), salyrgan (mersalyl and theophylline), and thiomerin (mercaptomerin) All contain about 39 per cent mercury in non-ionizable form, and all but thiomerin contain theophylline, which helps the absorption of the mercurial when given intramuscularly, decreases local irritation, and has a diuretic action itself. Thiomerin contains a sulfhydryl (mercapto) group instead of the theophylline

Mercuzanthin and salyrgan can be given intramuscularly or intravenously, but not subcutaneously. Mercuhydrin and thiomerin can be given subcutaneously, intramuscularly or intravenously

The effective dose varies from 0 5 to 2 cc Individual doses as large as 3 or 4 cc. have also been used but I do not recommend this In children, 0.5 cc. is adequate. The initial dose should be 0 25 cc for children, and 0 5 cc. for adults, after which it can be increased. Effective diuresis is indicated by a weight loss of two or three pounds

Cumertilin (Mercumatilin) is produced from the combination of mercurallylic acid, coumarin, and theophylline Each cc is equivalent to 39 mg. mercury and 50 mg theophylline Despite the fact that cumertilin is a coumarin derivative, it has no dicoumarol-like action on prothrombin formation.

The recommended dose of cumertilin is 1 cc intramuscularly. I have found it to have about one-half the diuretic effect of mercuhydrin

I prefer to use the mercurials once a week or less, and not more than 3 *times a week, because it has been my experience that when the patient does* not respond to three injections weekly, further injections will not be helpful and may be harmful The subcutaneous or intramuscular route is used *rather than the intravenous route, for reasons discussed on page 214*

Oral preparations of salyrgan, mercuzanthin, mercuhydrin with ascorbic acid, cumertilin and neohydrin are available I have obtained the best results with neohydrin Each tablet of neohydrin contains 18 mg of 3-chloro-mercuri-2-methoxy-propylurea, corresponding to 10 mg of mercury per tablet. From 1 to 6 tablets can be used daily given preferably at breakfast time I rarely have found it necessary to use more than 3 tablets a day

In cases of mild failure, one tablet can be given 3 or 4 times a week If abdominal cramps or diarrhea develop, the dose may have to be decreased or the drug stopped.

In cases of mild heart failure, the tablets may eliminate the need for mercurial injections; and in severe cases can prolong the interval between injections

Mercurial preparations in suppository form, such as mercuzan (mercuzanthin) and thiomerin suppositories are also available, but in my experience, *the rectal irritation that results* has prevented their prolonged use.

Mercurial Fastness.—With long-continued use of the mercurials, the kidneys may become refractory This usually happens in cases of severe fail-

calories (not necessarily a low-sodium diet), and have found that a weight loss of 1 to 1½ pounds a week can be accomplished without too much effort. To curb the appetite, benzedrine, 5 to 10 mg can be given after breakfast and lunch. I have found the following low-caloric diet satisfactory:

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Occasionally marked hyperpnea occurs immediately after an intravenous injection, and sometimes a chill and fever, urticaria or bronchial spasm may follow in about an hour.

3. *Dehydration and Electrolyte Disturbances*.—A good response to a mercurial is a diuresis of several liters. However, in some cases, massive diuresis of 13 or more liters in twenty-four hours may occur. Such diuresis may be dangerous for several reasons: the associated loss of sodium may cause marked thirst, weakness, abdominal cramps, muscular aches and cramps, and even collapse. In addition, other signs of dehydration, such as mental confusion, drowsiness, delirium, coma, a marked rise in temperature, and death may develop (see page 270).

The mobilization of large quantities of edema fluid may also result in digitalis toxicity if the patient has been receiving digitalis (see page 266). A sudden marked diuresis may also cause acute prostatic retention in elderly patients. Other electrolyte disturbances may cause tetany, with or without a decrease in the blood calcium level, hypochloremia and alkalosis, and an abnormal rise of the nonprotein nitrogen level of the blood. An attack of gout can even be precipitated by the mercurials.

4. *Mercurialism*.—Rarely, stomatitis, colitis, nephrosis and death due to mercurialism may occur in patients who have been receiving the injections over a long period of time. Fatal anuria may also occur as a result of the mercurials.

5. *Other Toxic Manifestations*.—Agranulocytosis occasionally occurs as a result of the mercurials. In such cases, a different mercurial can be substituted. In addition, BAL can be used to counteract the toxicity.

Other Diuretics.—**Ammonium Salts**.—Ammonium chloride and ammonium nitrate have a diuretic action and are able to increase the effectiveness of the mercurial diuretics. They act in the following way: the ammonium ion is metabolized to urea by the liver, the chloride or nitrate ion is excreted along with sodium and water by the kidneys. However, if the ammonium salt is administered for more than two days, ammonia is produced by the kidneys, and combines with the chloride or nitrate, so that the diuretic effect of the drug stops. For this reason ammonium salts must be used intermittently. The best results are obtained when they are given for two days preceding a mercurial injection. A large daily dose of approximately 6 to 12 grams (90 to 180 grains) in divided doses must be used. Uncoated tablets, rather than the enteric-coated tablets should be used, despite the gastric irritability which may result. The reason for this is that the enteric-coated tablets may not be absorbed.

Continued use of ammonium chloride beyond a period of several days may produce ammonium chloride poisoning and the high chloride syndrome (page 273).

The best results with ammonium chloride are obtained when it is used to potentiate the action of the mercurials in a patient who has heart failure but who does not have renal disease. In such a case, the ammonium chloride acts, not as a diuretic, but rather as a replacement for the loss of chloride resulting from the mercurials (page 252). Thus, when the ammonium chloride is given, the ammonia is converted to urea, but the chloride combines with a cation such as sodium and is excreted in the urine.

ure where the plasma chloride level is low and where the renal blood flow is also very low. Thus, even though the mercurial hinders reabsorption of sodium by the tubules, so little blood is flowing through the kidneys that diuresis is negligible. This can be overcome in several ways:

1. An intramuscular injection of the diuretic aminophylline (0.5 gram in a 2 cc ampoule) is given an hour after the mercurial. The aminophylline increases renal blood flow and so enables the mercurial to act more effectively.

2. The mercurial can be diluted with 10 cc decholin-sodium (sodium dehydrocholate), which itself is a mild diuretic, and injected intravenously.

3. For forty-eight hours prior to the injection, an acid-forming salt, such as 8 to 12 grams of ammonium chloride can be given orally in divided doses. However, this usually causes marked gastric distress, and it does not increase the diuresis very much.

4. Five grams of salt can be given daily for several days.

5. The mercurial injections can be stopped for a week or two, and another diuretic used. I have frequently found urea (page 254) effective in such cases. Potassium chloride (page 254) may also be helpful in such cases.

6. Morphine and demerol should not be given in conjunction with the mercurials because they interfere with the diuretic action of the mercurials.

7. If the patient has been ambulatory, he can be put to bed the day of the injection. The bed rest decreases the demands on the heart and increases the diuresis.

8. Pyridoxine, in a dose of 100 mg. can be injected along with the mercurial. The mode of action of pyridoxine is not known.

Contraindications to the Use of the Mercurial Diuretics.—The most important contraindication to the use of the mercurial diuretics is the inability of the kidneys to excrete the mercury. Thus, the mercurials should not be used in acute or subacute glomerular nephritis, or in the toxemias of pregnancy, or in uremia. The presence of ulcerative lesions of the gastrointestinal tract is also a contraindication to their use.

Toxic or Untoward Effects of the Mercurials.—The following toxic or untoward effects of the mercurials may occur:

1. *Local Effects.*—If, during an intravenous injection of salyrgan or mercuzanthin, some of the substance infiltrates the perivenous tissue spaces, marked pain, induration, and sometimes a slough may develop. A similar reaction may also occur with mercuhydrin or thiomerin if either is injected into edematous or adipose tissue. The intramuscular injection of the mercurials may also be very painful. This can be eliminated by diluting the mercurial with 1 cc. of a 2 per cent novocaine solution.

2. *Immediate Toxic Reactions.*—The intravenous injection of the mercurials has been responsible for sudden and almost immediate death in several instances, probably due to the development of ventricular fibrillation. In most of these fatal cases, the injection had been given very rapidly, or the patient had become refractory to the mercurial, which was being given in shorter intervals and in progressively larger doses. However, only one case of sudden death has been reported after intramuscular administration.

Occasionally marked hyperpnea occurs immediately after an intravenous injection, and sometimes a chill and fever, urticaria or bronchial spasm may follow in about an hour.

3. *Dehydration and Electrolyte Disturbances.*—A good response to a mercurial is a diuresis of several liters. However, in some cases, massive diuresis of 13 or more liters in twenty-four hours may occur. Such diuresis may be dangerous for several reasons: the associated loss of sodium may cause marked thirst, weakness, abdominal cramps, muscular aches and cramps, and even collapse. In addition, other signs of dehydration, such as mental confusion, drowsiness, delirium, coma, a marked rise in temperature, and death may develop (see page 270).

The mobilization of large quantities of edema fluid may also result in digitalis toxicity if the patient has been receiving digitalis (see page 266). A sudden marked diuresis may also cause acute prostatic retention in elderly patients. Other electrolyte disturbances may cause tetany, with or without a decrease in the blood calcium level, hypochloremia and alkalosis, and an abnormal rise of the nonprotein nitrogen level of the blood. An attack of gout can even be precipitated by the mercurials.

4. *Mercurialism.*—Rarely, stomatitis, colitis, nephrosis and death due to mercurialism may occur in patients who have been receiving the injections over a long period of time. Fatal anuria may also occur as a result of the mercurials.

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However, if the heart failure is severe and the patient is on a rigid low sodium diet, very little sodium passes through the kidneys. The chloride is excreted, not as sodium chloride, but mostly as ammonium or potassium chloride. In such a case, the duretic value of ammonium chloride is negligible. In addition, the drug may produce a serious depletion of potassium from the body.

The Xanthine Diuretics.—These act by increasing the glomerular filtration rate and possibly by decreasing the tubular reabsorption of water. They are effective diuretics but must be given in large doses orally. They cause gastric distress, and tolerance develops after a few days.

Theophylline can be given in a dose of 0.3 gram, 3 to 5 times daily, or in the form of a double salt, such as theophylline with calcium salicylate, or theophylline ethylene diamine (aminophylline), 0.5 gram, 3 to 5 times daily.

Theobromine and its double salt mixtures are less effective than theophylline and its compounds, but can also be used. The dose of theobromine is 0.6 gram, 3 to 5 times daily. The dose of theobromine sodium acetate, or of theocalcin (theobromine calcium salicylate) is 1 gram, 3 to 5 times daily. Theobromine sodium acetate should not be used for long periods because of the presence of the sodium ion.

Theophylline and theobromine compounds are available in enteric-coated pills of 0.5 gram (7½ grain) strength.

Urea.—Urea is a very effective diuretic, though very unpleasant to take. It produces diuresis because the tubules reabsorb only about 40 per cent of the urea that passes through the glomeruli, and the excess urea is excreted with the water in which it is dissolved. Since large doses of urea can be given orally, marked diuresis may occur. Urea should not be used in cases of chronic kidney disease with nitrogen retention, but the elevated nitrogen level which occurs with congestive heart failure is not a contraindication to its use.

Daily doses of 60 to 90 grams should be used. The drug can be prepared as a 50 per cent solution, and imbibed cold. Or it can be prescribed in crystal form, the daily dose of 4 to 6 tablespoons being freshly dissolved in iced water or fruit juice to mask the taste.

Bismuth.—Bismuth sodium tartrate, in a dose of 0.03 gram (½ grain) injected intramuscularly may lead to diuresis that persists from four to eighteen days. It has no toxicity. The exact mechanism of its action is unknown.

Potassium Salts.—Although the renal tubules act to conserve sodium, potassium is very rapidly excreted, and when given in large amounts acts as a good diuretic. Potassium chloride is usually used, though any of the other potassium salts can be used equally well. The daily dose is 5 to 10 grams (75 to 150 grains). It can be given in divided doses in the form of capsules, tablets or in solution. I have found a 25 per cent solution of potassium chloride in syrup of orange effective. (One dram is equivalent to approximately 1 gram of the salt.) Oral Potassium Triplex Solution (Lilly), which supplies approximately the same amount of potassium (5 cc supplies 15 mEq. potassium) is also palatable. Potassium chloride can also be used as a salt substitute for sprinkling on food. The only contraindication to the use of potassium is severe renal disease, because if the

potassium is not excreted, muscular and nerve paralysis and death may occur

When potassium is used as a diuretic, its action should be checked periodically with the electrocardiogram or with serum potassium analyses (see page 207).

Water.—Even water can be used as a diuretic, in conjunction with a low-sodium diet, because when imbibed in large quantities it depresses the posterior pituitary, causing decreased tubular reabsorption of water, and diuresis

Carbonic Anhydrase Inhibitors—Carbonic anhydrase inhibitors induce a diuresis like ammonium chloride In other words, they produce an acidosis However, the carbonic anhydrase inhibitors such as diamox and dirnate are not acidifying salts but are sulfonamide derivatives which affect the bicarbonate enzyme system through the body This system consists of *the intracellular conversion of CO_2 and H_2O to H_2CO_3 and H ion and is* mediated by the enzyme, *carbonic anhydrase* In the cells of the kidney tubules, the H ions normally exchange with Na and K ions from the urinary filtrate This is responsible for a considerable proportion of the total sodium and potassium reabsorbed by the kidneys When carbonic anhydrase is inhibited, the hydration of CO_2 is also inhibited This reduces the availability of H ion for exchange with Na and K. Thus, H ions are retained and the Na and K which would normally be reabsorbed are excreted in the urine, together with a proportionate amount of water

The retention of the H ions produces a metabolic acidosis in association with the diuresis which occurs Because of this acidosis, the carbonic anhydrase inhibitors can only be used intermittently, such as every other day, to allow the acidosis to disappear and sodium and water to reaccumulate in the body In addition, the concomitant use of acidifying salts such as ammonium chloride or of resins which produce an acidosis, is contraindicated However, the carbonic anhydrase inhibitors can be used with the mercurials.

Diamox (Acetazoleamide) is marketed in tablets of 250 mg strength The average dose is one tablet, at breakfast, every other day The diuretic effect is mild, compared to the mercurials

Drowsiness, and paresthesias may occur as side reactions Disorientation has been observed in cases of cirrhosis of the liver In addition, drug fever has been reported (probably due to the sulfonamide structure of the compounds) Since the carbonic anhydrase inhibitors have essentially no effect on chloride excretion, the hypochloremia occasionally seen with prolonged mercurial treatment, does not occur.

The carbonic anhydrase inhibitors are effective particularly in cases of cor pulmonale due to emphysema and chronic pulmonary fibrosis with CO_2 retention The reason for this is that the inhibitors increase the excretion of the bicarbonate ion However, they are contraindicated in cases of renal impairment and in cirrhosis of the liver

4. **Digitalis Preparations.**—The active principles of digitalis and of drugs with a digitalis-like action are known as glycosides. Each cardiac glycoside consists of a sterol-like cyclic compound called aglycone or genin, combined with a sugar molecule or a chain of sugar molecules. The aglycones are similar in chemical structure to cholesterol and the sex hormones The

sugar components contain specific sugars such as digitoxose and cymarose, and nonspecific sugars such as rhamnose and glucose. From each naturally occurring glycoside, additional glycosides can be formed by enzymatic action or mild acid or alkaline hydrolysis, until finally a simple aglycone remains. Although the pharmacological activity resides in the aglycone, the sugars control the solubility and the duration of action of the drug, so that the glycoside is more powerful than the aglycone.

From the leaf of the purple-flowered digitalis purpurea the glycosides digitoxin, gitalin, and gitoxin can be derived. The yellow-flowered digitalis lanata contains the naturally occurring glycosides, lanatoside A, lanatoside B, and lanatoside C. When these are hydrolyzed, the glycosides digitoxin, gitoxin and digoxin, respectively are formed. Thus, digitoxin can be derived from either digitalis purpurea or lanata, but digoxin is obtained only from digitalis lanata.

From the seed of the African plant strophanthus kombe (strophanthus K) the glycosides strophanthin K and strophanthoside K are obtained, and from the seed of the strophanthus gratus (strophanthus G), ouabain is obtained. From the dried fleshy bulb of white maritima squill, the glycosides urginin A and B, and scillarin A and B are obtained.

For therapeutic purposes, the most commonly used preparations are the powdered leaf preparations of digitalis purpurea, and the glycosides, digitoxin, digoxin, lanatoside C, ouabain and strophanthin K. All the digitalis and digitalis-like products have similar pharmacological properties, differing only in speed of action, degree of absorption from the gastrointestinal tract and rate of dissipation. Therefore I shall first describe the action of the glycosides in general, and then will consider the characteristics of the individual preparations.

The Effect of Digitalis on the Cardiovascular System.—Cardiac muscle is much more sensitive to the cardiac glycosides than the other muscles of the body, and when the glycoside enters the cell and splits to form the active aglycone, it produces a marked increase in the efficiency of the heart muscle.

Digitalis has a direct effect on the heart muscle. On page 232 I described the physiochemical mechanism of muscular contraction. Digitalis affects this favorably in many ways. It can accelerate the spiraling of the myosin threads. It also accelerates the polymerization of actin, preliminary to the union of actin with myosin. In addition, digitalis in therapeutic doses increases the concentration of potassium in the heart muscle cells. This also increases the strength of cardiac contraction. (Toxic doses of digitalis cause the heart muscle cells to lose potassium.)

Digitalis increases the mechanical efficiency of the heart without an associated change in diastolic length, and in addition, the heart is able to do a given amount of work with less oxygen consumption. The effects of digitalis on heart rate, heart size, venous pressure, cardiac output are for the most part secondary to its direct effect on the heart muscle. When the mechanical efficiency of the heart improves, the cardiac output rises, circulation through the kidney improves, edema fluid is excreted, and the venous pressure falls.

It has been recently claimed that digitalis lowers the venous pressure directly by means of reflexes from the central nervous system and not as a

result of the effect of the drug on the heart. This may explain the fact that in a normal person, digitalis decreases the venous pressure, the cardiac output and the size of the heart, the sequence of events possibly being. decreased venous pressure, decreased return of blood to the heart, decreased cardiac output and decreased heart size.

Digitalis can cause the heart rate to slow in several ways· Slowing may take place as a compensatory mechanism when the cardiac output improves Digitalis can also affect the heart rate especially in cases of auricular fibrillation by virtue of its depressive effect upon the conduction system of the heart, and as a result of vagal stimulation In auricular fibrillation, about 400 stimuli from the auricles reach the *a–v* node per minute Many of these stimuli are spontaneously blocked, but enough can pass so that the ventricular rate may be very high However, after digitalization, most of the stimuli are blocked at the *a–v* node, and the ventricular rate usually drops dramatically Digitalis also acts on the *a–v* node by way of the vagus nerve When digitalis is given to a normal person, its effect on the heart rate is minimal, and I have seen the rate actually increase a few beats

The marked diuretic action that often follows the administration of digitalis is solely due to its beneficial effect on the heart, and no diuresis occurs when digitalis is given to a normal person or to a patient with a fluid accumulation of noncardiac origin.

Along with its effect on the mechanical efficiency of the heart, digitalis causes characteristic changes in the electrocardiogram, consisting of a decreased $Q–T$ interval, a decrease in the amplitude of T, reversal of the direction of T, and finally fusion of the T wave with the $RS–T$ segment which is displaced in a direction opposite to that of the QRS complex (see page 203)

Toxic electrocardiographic changes are described on page 265 The effects of digitalis on paroxysmal tachycardia, auricular flutter and auricular fibrillation are described under these topics.

Should Digitalis Be Given in All Cases of Congestive Heart Failure?—Digitalis is indicated in most but not all cases of congestive heart failure It has its greatest usefulness in cases of low-output failure In high-output failure, due to chronic pulmonary disease, hyperthyroidism, *etc*, the results with digitalis are generally but not always poor Digitalis is also ineffective in patients with right-sided failure due to pericardial effusion or chronic constrictive pericarditis

Similarly, in cases of acute rheumatic fever or infectious carditis, digitalis is usually not effective As a matter of fact, severe toxicity, including auricular fibrillation, *a–v* block and even death can occur from relatively small doses of digitalis given to children suffering from heart failure due to acute rheumatic carditis Therefore it is much safer to try to control the failure in such cases with oxygen, mercurial and xanthine diuretics, a low-sodium diet, and the salicylates, (which may accelerate resorption of pleural and pericardial effusions) If digitalis is used, small doses should be given, and careful observations, including repeated electrocardiograms made for the occurrence of arrhythmias

Digitalization —The current method of prescribing digitalis preparations is to give a large initial dose or doses to produce digitalization, and then to continue with smaller maintenance doses Digitalization can be described

sugar components contain specific sugars such as digitoxose and cymarose, and nonspecific sugars such as rhamnose and glucose. From each naturally occurring glycoside, additional glycosides can be formed by enzymatic action or mild acid or alkaline hydrolysis, until finally a simple aglycone remains. Although the pharmacological activity resides in the aglycone, the sugars control the solubility and the duration of action of the drug, so that the glycoside is more powerful than the aglycone.

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It has been recently claimed that digitalis lowers the venous pressure directly by means of reflexes from the central nervous system and not as a

When given orally, it is only partially absorbed from the gastrointestinal tract, and at least 1.5 mg. must be used for digitalization. This can be given in 2 doses at six hour intervals. The maintenance oral dose averages 0.5 mg. (0.25 to 0.75 mg.). Regardless of the route of administration, digoxin is excreted in about three days. Thus, if toxicity occurs, it disappears in several hours or a day.

Digoxin is supplied as 0.25 mg. tablets for oral use, and in solution for undiluted intramuscular or intravenous use. The solution has 0.25 mg. digoxin per cc. in an aqueous mixture of 10 per cent alcohol and 40 per cent propylene glycol. Each ampoule therefore contains 2 cc. (0.5 mg. digoxin). An initial dose is 0.5 to 1 mg. An additional dose of 0.25 to 0.5 mg. can be given at six hour intervals. Digitalization requires 1 to 1.5 mg.

3. *Strophanthus Preparations.*—Ouabain is the glycoside obtained from strophanthus-G. It is the most potent and quickly acting of all the cardiac glycosides, and therapeutic effects can be noted within five minutes after intravenous injection. The therapeutic dose is 0.25 mg. Most of the drug is dissipated within one day. Since ouabain is poorly absorbed from the gastrointestinal tract, it cannot be given orally.

Because of its extremely rapid action it should not be used if the patient has had any digitalis preparation in the past week. In a doubtful case, a dose of 0.1 mg. or even 0.05 mg. can be given. It should be administered slowly, and can be diluted with 10 cc. sterile isotonic saline or distilled water, or with 10 cc. aminophylline. The dose can be repeated in six hours.

Ouabain is now used infrequently in this country because of numerous deaths which have occurred from it in the past. In the dosage described above, it is safe and very effective. However, practically the same rapid digitalization can be obtained with lanatoside C or with digoxin, which are much safer.

Strophanthin-K and K-strophanthoside contain the purified glycosides of strophanthus-K. Their action and dosage are similar to that of ouabain. Another similar preparation is acetyl-strophanthidin. This is not a glycoside but an aglycone.

B. **Slowly-Acting Digitalis Preparations.**—These include: (1) digitalis purpurea and digitalis lanata leaf preparations, and (2) digitoxin.

1. *Digitalis Purpurea Leaf Preparations.*—The powdered dry leaf preparations and the official tincture (10 per cent) are poorly and incompletely absorbed from the gastrointestinal tract (only about one-fifth of the oral dose is absorbed). In addition, there is a latent period of several hours before therapeutic effects are noted, even when the preparations of the leaf are given intravenously. Dissipation is slow, toxicity may last a week or more, and effects of the drug on the electrocardiogram can be noted as long as four weeks after the drug has been stopped.

Standardization of Digitalis Leaf Preparations.—Because digitalis leaf preparations contain a mixture of glycosides in unknown proportions, biological standardization has been necessary. Digitalis leaf is now so prepared that 0.1 gram of U.S.P. XIII digitalis is the equivalent of 1 unit.

The strength of the U.S.P. unit of digitalis has changed in successive editions of the Pharmacopœia, the unit of U.S.P. XII (1942) and U.S.P. XIII (1947) being weaker than that of U.S.P. XI (1936), but stronger than

as the uptake of the drug by the heart until a maximum therapeutic effect is obtained, or until toxic symptoms develop. It is extremely difficult to determine when full digitalization has been obtained. In cases of auricular fibrillation, a fall of the ventricular rate to about 70 is a fairly good sign of digitalization, but in patients with heart failure and normal rhythm, the heart rate cannot be used as a guide. The improvement in the patient's condition with relief of dyspnea and of the other symptoms, the onset of diuresis, loss of edema fluid and weight, *etc.*, can be used only if no other therapeutic procedure but digitalis had been employed. However, most patients also receive in addition to digitalis, diuretics, a low-sodium diet, and bed rest, all of which are very helpful. Another difficulty in dosage is that many of the toxic effects of digitalis are merely extensions of its therapeutic actions For these reasons, I would prefer to underdigitalize rather than overdigitalize a patient in congestive heart failure, using additional measures to control the heart failure.

Digitalis Preparations in Clinical Use.—Inasmuch as all digitalis preparations possess similar pharmacological properties, one might ask why it is necessary to use more than one. The answer is that various preparations of the leaf and glycosides differ in the completeness and quickness of absorption from the gastrointestinal tract, in their latent period, even when given intravenously, and in the rate of their dissipation from the body (Table 4).

In a general way, digitalis preparations can be divided into two groups:

A. **Rapidly-Acting Digitalis Preparations.**—These include: (1) lanatoside C, (2) digoxin, (3) ouabain and other strophanthus preparations. These preparations act within a few minutes when given intravenously, and are eliminated from the body in from one to three days.

1 *Lanatoside C (Cedilanid—D)* —Lanatoside C is one of the glycosides derived from digitalis lanata When given intravenously, there is a very short latent period of about ten minutes This makes lanatoside C excellent for rapid digitalization. The average digitalizing dose is from 1.2 to 1.6 mg (6 to 8 cc.).

When given orally, only a small portion of it is absorbed from the gastrointestinal tract so that a large digitalizing dose of 7 mg. by mouth must be used. This is given in 3 divided doses at six-hour intervals. If slower digitalization over a period of seventy-two hours is used, as much as 10 mg. or more may be needed. The latent period after oral administration is several hours

Regardless of the route of administration, lanatoside C is dissipated in about three days. Thus, if toxicity occurs, it disappears in several hours or a day. I have occasionally given a full digitalizing dose of 1 6 mg. intravenously to a patient who had been previously digitalized and was taking a maintenance dose of digitalis powder, with either no toxic symptoms developing or only transient nausea or vomiting for a few hours.

Lanatoside C is marketed under the trade-name Cedilanid—D. It is prepared in tablets of 0 5 mg. strength, and in 2 cc. and 4 cc. ampoules, containing 0.4 and 0.8 mg respectively.

2. *Digoxin.*—Digoxin is a breakdown product of lanatoside C, and its properties are very similar to it. When given intravenously in a dose of 1 mg., its latent period is even slightly shorter than that of lanatoside C.

When given orally, it is only partially absorbed from the gastrointestinal tract, and at least 1.5 mg. must be used for digitalization. This can be given in 2 doses at six hour intervals. The maintenance oral dose averages 0.5 mg. (0.25 to 0 75 mg.). Regardless of the route of administration, digoxin is excreted in about three days. Thus, if toxicity occurs, it disappears in several hours or a day.

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Standardization of Digitalis Leaf Preparations.—Because digitalis leaf preparations contain a mixture of glycosides in unknown proportions, biological standardization has been necessary. Digitalis leaf is now so prepared that 0 1 gram of U.S.P. XIII digitalis is the equivalent of 1 unit.

The strength of the U.S.P. unit of digitalis has changed in successive editions of the Pharmacopœia, the unit of U.S P. XII (1942) and U.S.P. XIII (1947) being weaker than that of U.S.P. XI (1936), but stronger than

as the uptake of the drug by the heart until a maximum therapeutic effect is obtained, or until toxic symptoms develop. It is extremely difficult to determine when full digitalization has been obtained. In cases of auricular fibrillation, a fall of the ventricular rate to about 70 is a fairly good sign of digitalization, but in patients with heart failure and normal rhythm, the heart rate cannot be used as a guide. The improvement in the patient's condition with relief of dyspnea and of the other symptoms, the onset of diuresis, loss of edema fluid and weight, *etc*, can be used only if no other therapeutic procedure but digitalis had been employed. However, most patients also receive in addition to digitalis, diuretics, a low-sodium diet, and bed rest, all of which are very helpful. Another difficulty in dosage is that many of the toxic effects of digitalis are merely extensions of its therapeutic actions. For these reasons, I would prefer to underdigitalize rather than overdigitalize a patient in congestive heart failure, using additional measures to control the heart failure

Digitalis Preparations in Clinical Use.—Inasmuch as all digitalis preparations possess similar pharmacological properties, one might ask why it is necessary to use more than one. The answer is that various preparations of the leaf and glycosides differ in the completeness and quickness of absorption from the gastrointestinal tract, in their latent period, even when given intravenously, and in the rate of their dissipation from the body (Table 4).

In a general way, digitalis preparations can be divided into two groups:

A. **Rapidly-Acting Digitalis Preparations.**—These include: (1) lanatoside C, (2) digoxin; (3) ouabain and other strophanthus preparations. These preparations act within a few minutes when given intravenously, and are eliminated from the body in from one to three days.

1. *Lanatoside C (Cedilanid—D)* —Lanatoside C is one of the glycosides derived from digitalis lanata. When given intravenously, there is a very short latent period of about ten minutes. This makes lanatoside C excellent for rapid digitalization. The average digitalizing dose is from 1.2 to 1.6 mg. (6 to 8 cc.).

When given orally, only a small portion of it is absorbed from the gastrointestinal tract so that a large digitalizing dose of 7 mg. by mouth must be used. This is given in 3 divided doses at six-hour intervals. If slower digitalization over a period of seventy-two hours is used, as much as 10 mg. or more may be needed. The latent period after oral administration is several hours

Regardless of the route of administration, lanatoside C is dissipated in about three days. Thus, if toxicity occurs, it disappears in several hours or a day. I have occasionally given a full digitalizing dose of 1.6 mg. intravenously to a patient who had been previously digitalized and was taking a maintenance dose of digitalis powder, with either no toxic symptoms developing or only transient nausea or vomiting for a few hours.

Lanatoside C is marketed under the trade-name Cedilanid—D. It is prepared in tablets of 0.5 mg. strength, and in 2 cc. and 4 cc. ampoules, containing 0.4 and 0.8 mg. respectively.

2. *Digoxin.*—Digoxin is a breakdown product of lanatoside C, and its properties are very similar to it. When given intravenously in a dose of 1 mg., its latent period is even slightly shorter than that of lanatoside C.

Puriti	Variable—Saponins, fats, impurities, etc Standardized—Bioassay—cat, U S P units, etc	Relatively pure—Up to 90–95% Standardized by wt and bioassay	Chemically pure—Standardized by wt	Chemically pure—Standardized by wt
Oral Absorption	Poor	Practically complete	Fairly complete	Poor
Speed of Action I V	Slow	Relatively slow Max effect 6–10 hrs	Rapid—5–10 mins Max effect 1–2 hrs	Rapid—5–10 mins Max effect 1–2 hrs
Speed of Action oral	Slow—4–6 hrs Max effect 24–36 hrs	Slow—4–6 hrs Max effect 10–12 hrs	Fast—1–2 hrs Max effect 6–7 hrs	Irregular absorption Maximum effect 8–9 hrs
Duration of Action	Long—2–3 weeks	Long—2–3 weeks	Short—3–4 days	Short—3–4 days
Toxic Effects	Great—Lasts long	Great—Lasts long	Low—Shorter duration	Low—Shorter duration
Digitalizing Dose I V	—	1 2 mg	1 0 mg	1 6 mg
Digitalizing Dose oral	1 2 grams	1 2 mg	1 5 mg	7 0 mg
Maintenance Dose oral	0 10 gram	0 1 mg	0 5 mg	0 5—1 mg

TABLE 4.—THE PHARMACOLOGY OF SOME OF THE MORE COMMON DIGITALIS PREPARATIONS

	Digitalis—Whole leaf	*Digitoxin*	*Digoxin*	*Lanatoside C*
PREPARATIONS	Digitalis leaf— Digalen—Hoffman la Roche Digitan—Merck Digitol—Sharpe & Dohme Digifolin—Ciba Digifortis—Parke-Davis	Digitaline Nativelle—Varick Digitoxin—Squibb Purodigin—Wyeth Crystodigin—Lilly	Digoxin—Burroughs, Wellcome & Co	Cedilanid—Sandoz
DERIVATION	*Dig Purpurea*	*from Dig Purpurea or Lanata*	*from Dig Lanata*	*from Dig Lanata*
FORMULA	Mixture of glycosides, etc Relatively impure, variable	O, =O, CH_3, CH_3, OH HO—$C_6H_{10}O_3$—$C_6H_{10}O_3$—$C_6H_{10}O_3$ $C_{41}H_{64}O_{13}$	O, =O, OH, CH_3, CH_3, OH HO—$C_6H_{10}O_3$—$C_6H_{10}O_3$—$C_6H_{10}O_3$ $C_{41}H_{64}O_{14}$	O, =O, OH, CH_3, CH_3, OH HO—$C_6H_{10}O_3$—$C_6H_{10}O_3$—$C_6H_{10}O_3$ + $C_6H_{12}O_6$ + CH_3COOH $C_{49}H_{76}O_{20}$

PURITY		Variable—Saponins, fats, *impurities*, etc Standardized—Bioassay—cat, U S P units, etc	Relatively pure—Up to 90–95% Standardized by wt and bioassay	Chemically pure—Standardized by wt	Chemically pure—Standardized by wt
ORAL ABSORPTION		Poor	Practically complete	Fairly complete	Poor
SPEED OF ACTION	I V	Slow	Relatively slow Max effect 6–10 hrs	Rapid—5–10 mins Max effect 1–2 hrs	Rapid—5–10 mins Max effect 1–2 hrs
	oral	Slow—4–6 hrs Max effect 24–36 hrs	Slow—4–6 hrs Max effect 10–12 hrs	Fast—1–2 hrs Max effect 6–7 hrs	Irregular absorption Maximum effect 8–9 hrs
DURATION OF ACTION		Long—2–3 weeks	Long—2–3 weeks	Short—3–4 days	Short—3–4 days
TOXIC EFFECTS		Great—Lasts long	Great—Lasts long	Low—Shorter duration	Low—Shorter duration
DIGITALIZING DOSE	I V	—	1 2 mg	1 0 mg	1 6 mg
	oral	1 2 grams	1 2 mg	1 5 mg	7 0 mg
MAINTENANCE DOSE	oral	0 10 gram	0 1 mg	0 5 mg	0 5 – 1 mg

that of U.S.P. X (1926). Thus, 1 gram of U.S.P. XIII digitalis is equivalent to 0.83 gram of U.S.P. XI digitalis, and to 1.33 gram of U.S.P. X digitalis. The importance of this is that references to digitalis dosage in the literature prior to 1936 refer to the weak U.S.P. X standard.

A further source of confusion with respect to digitalis unitage concerns the term cat-unit. A cat-unit is determined by the method of Hatcher and Brody and is the weight of the dry drug in milligrams necessary to kill one kilogram of cat, when given slowly and continuously by the intravenous route. By chance, 1 cat-unit of digitalis leaf preparations was contained in 0.1 gram (1½ grains) of U.S.P. X digitalis powder, or in 1 cc. U.S.P. X tincture. Thus, it was customary for many years to convert cat-units directly into gram and cc. doses of the drug. However, with the increased potency of the U.S.P. XI, XII and XIII digitalis units, this simple relation between cat-units and dosage was lost, and at the present time, although digitalis is still standardized using a modification of the Hatcher-Brody cat method, the term cat-unit is no longer used for clinical purposes.

Digitalization with digitalis leaf can be accomplished in the following way. 0.06 to 0.1 gram (1 to 1½ grains) of powdered leaf should be given for every 10 pounds of body weight, the full dose being given within twenty-four hours. Thus, for a 150 pound adult, 1.2 grams (18 grains) can be given in 3 divided doses, six hours apart. A very heavy person may need more, a light person, less of the drug. For rapid digitalization, digitalis leaf should not be used, but rather, one of the quick-acting glycosides (page 258). Digitalization with the tincture of digitalis can be accomplished, using 0.6 to 1 cc. (10 to 15 minims) for every 10 pounds of body weight.

Maintenance of digitalization can be accomplished with 0.06 to 0.1 gram (1 to 1½ grains) of digitalis leaf powder, or 0.6 to 1 cc. (10 to 15 minims) of the tincture daily.

Digitalis is usually supplied in 0.06 and 0.1 gram (¾ and 1½ grain) tablets, and in the form of the 10 per cent tincture.

2. *Digitoxin.*—The glycoside digitoxin has the property of being almost completely absorbed from the gastrointestinal tract unlike digitalis leaf and the other glycosides. However, its latent period is long, being at least an hour, even when it is injected intravenously, and its rate of dissipation is very slow, the drug remaining in the body for several weeks after it is discontinued. Because of this and the fact that it is so well absorbed from the gastrointestinal tract, a patient who becomes toxic, may continue to show signs of toxicity a week or longer after the drug has been stopped.

Studies with radioactive digitoxin have shown that minute quantities of it can be detected in the body even forty days after a single dose. In addition, breakdown products of the digitoxin can be detected in the body for seventy-four days after a single dose.

The average digitalizing dose of digitoxin is about 1.2 mg. which can be given in 1 dose, or in 2 doses, at six-hour intervals. Although a digitalizing dose as high as 2.2 mg. has been recommended by some, I prefer to use the smaller dose, which may in some cases be excessive. The average maintenance dose is 0.1 mg. Digitoxin can be given intravenously in a dose of 1.2 mg., but because of its comparatively long latent period, it is not the drug of choice when rapid digitalization is required.

Digitoxin is now prepared in tablets of 0.05 mg., 0.1 mg., 0.15 mg. and 2 mg. strength, and in 1 cc. ampoules containing 0.2 mg.

3. *Gitaligin* (Gitalin).—Amorphous gitalin, one of the glycosides of digitalis purpurea, is now available for oral use. It is excreted from the *body probably within a week, more slowly than digoxin or lanatoside C*, but much more rapidly than digitoxin.

It is supplied in tablets of 0.5 mg strength. The average digitalizing dose is 6 mg., given over a period of four days (3 tablets daily). The average maintenance dose is 0.5 mg. (1 tablet) daily. However, one must remember that marked individual variations in sensitivity can occur with gitalin as with any of the other digitalis glycosides.

Digitalis Dosage for Children and Infants.—Children require about one-half the adult dose of digitalis preparations. In many cases, children appear to be refractory to digitalis and seem to require proportionately larger doses than adults. One explanation for this is that heart failure in children is usually due to rheumatic carditis, which responds poorly to digitalis.

TABLE 5.—DOSAGE OF DIGITALIS PREPARATIONS FOR INFANTS

Digitalis Preparation	*Administration*	*Digitalizing Dose*	*Maintenance Dose*
Digoxin	Oral, IM, IV	0.125 mg per 7 lbs (3 Kg.) wt	10% of digitalizing dose
Lanatoside C	IM, IV	0.2 mg per 7 lbs weight	"
Digitoxin	Oral IM, IV	0.1 mg per 7 lbs weight	"
Digitalis leaf	Oral	0.1 gram per 7 lbs weight	"
Tr. digitalis	Oral	1 cc. per 7 lbs weight	"

Infants require a different dose schedule (Table 5). For parenteral injection, half the digitalizing dose can be given at once and repeated in two hours. When digitalis is used orally, the method of administration is similar to that used for adults.

The Choice of a Digitalis Preparation.—For rapid intravenous digitalization, I ordinarily use lanatoside C, and for oral digitalization and maintenance, digoxin. However, tablets of lanatoside C, digitoxin or digitalis leaf powder are also satisfactory for oral use. If digitalis leaf or digitoxin is being used and toxicity occurs, the drug should be stopped and after a suitable rest period of at least a week, the patient should be placed on either *digoxin or lanatoside C, which is rapidly excreted. If the patient becomes* toxic while taking lanatoside C or digoxin, the drug should be stopped for two or three days and then continued in smaller doses.

There are available digitalis preparations other than those I have described above, but they offer no advantages over the standard preparations.

How Quickly Shall the Patient Be Digitalized?—Physicians for many years were accustomed to digitalize a patient over a period of several days to a week, using digitalis leaf preparations. One reason for this was that the latent period of the digitalis is at least six hours, absorption uncertain, the various leaf preparations vary greatly in potency, and once toxicity develops it persists for some time. However, with the use of the rapidly acting and

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Digitalis should not be used prophylactically, even preoperatively, in a patient with organic heart disease, if no signs of heart failure have ever been present. Similarly, digitalis should not be given to patients to control a sinus tachycardia due to any cause other than congestive heart failure, notwithstanding the fact that digitalis is effective in abolishing attacks of paroxysmal tachycardia.

The presence of acute myocardial infarction, angina pectoris, glomerular nephritis, bundle branch block, incomplete or even complete *a–v* block are not contraindications to the use of digitalis, if congestive heart failure is present. In fact, I have observed instances where complete *a–v* block disappeared in a patient with congestive heart failure when compensation was restored. Similarly, although premature auricular and ventricular contractions may result from digitalis toxicity, digitalis may cause these arrhythmias to disappear (even if the patient does not have congestive heart failure).

Digitalis Toxicity.—Every preparation of digitalis or of the cardiac glycosides which exerts a therapeutic effect will produce toxic effects if given in sufficiently large doses.

Gastrointestinal Disturbances.—The most common of these are nausea and vomiting, usually in that order Copious salivation also occasionally occurs, as does diarrhea. The nausea and vomiting are due for the most part to irritation of the vomiting center in the medulla, because, in animals, retching movements of the diaphragm and abdominal wall occur after digitalization, even when the stomach is removed. However, there is also probably some local irritative effect on the stomach because the glycosides produce nausea and vomiting less frequently than the powder

Visual and Central Nervous System Disturbances.—White halos may appear around dark objects (white vision), or objects may appear yellow and green, (yellow vision) sometimes, red and blue. Transient amblyopia, scotomata and even retrobulbar neuritis may develop.

In addition, headache, disorientation, hallucinations, delirium and coma may occur. These symptoms are very serious and are due in part to the marked dehydration which many of the patients develop because of the persistent vomiting.

Cardiac Disturbances.—The most common toxic sign referable to the cardiovascular system is the appearance of ventricular premature contractions, which may occur as isolated premature beats but which more usually appear after alternate normal beats, producing a bigeminal rhythm and coupling of the pulse. The premature ventricular contractions may arise from a single or from multiple foci If the digitalis is not stopped, ventricular tachycardia may develop. The electrocardiogram may show the usual ventricular tachycardia, or a bidirectional ventricular tachycardia—alternate *QRS* complexes point in the opposite direction.

Digitalis toxicity can also produce multiple auricular premature contractions or paroxysmal auricular tachycardia, especially an auricular tachycardia with *a–v* block. Auricular fibrillation or auricular flutter can also occur as toxic manifestations of digitalis.

Digitalis can also cause sinus arrest, and various degrees of *a–v* block. The most common is a prolonged *P–R* interval, but the Wenckebach type

effectively absorbed preparations of uniform potency, it is not necessary to prolong unduly the process of digitalization. One disadvantage of digitalization over a period of several days is that the total dose of the preparation used must be increased because a portion of the drug is excreted or destroyed in the body over a period of days. Thus, it *may require 2 grams* or more of digitalis leaf to digitalize a patient over a period of three days whereas 1.2 grams may be sufficient when digitalization is done within one day Similar relations hold when the glycosides are used.

My practice is to digitalize the patient within twenty-four hours if obvious signs of heart failure are present, using the dosage and preparations described in the preceding pages. However, if the patient is ambulatory and is in mild heart failure, slow digitalization can be done over a period of a week or more by prescribing 0 75 mg. digoxin, or 2 mg lanatoside C, or 0.2 gram (3 grains) digitalis leaf, or 0 2 mg digitoxin daily until clinical signs of digitalization occur, or signs of toxicity appear, at which time, a maintenance dose can be prescribed

How Long Shall Digitalis Therapy Be Maintained?—No specific answer can be given this question A patient with rheumatic mitral stenosis, auricular fibrillation and chronic right- and left-sided failure may require digitalis the remainder of his life. On the other hand, a patient in mild failure may be able to discontinue digitalis within a few weeks, provided his condition remains improved on a low-sodium diet. The only real danger from continued digitalis therapy is that a cumulative effect may occur even with maintenance doses, with the eventual development of toxicity.

There has been a tendency for the physician to use digitalis as the primary therapeutic measure in the treatment of chronic heart failure. This *has become a dangerous practice since the advent of the powerful glycosides*, especially digitoxin, which is absorbed so well from the gastrointestinal tract, because the toxicity which develops with digitoxin may last almost two weeks and may lead to death. In this connection I have on more than one occasion witnessed the following: Patient develops severe heart failure and is digitalized with digitoxin: failure persists: more digitoxin: patient begins to vomit and becomes weaker (because of beginning dehydration), but is given more digitoxin because the physician thinks it is not being absorbed· more vomiting· more digitoxin, this time intramuscularly. high fever, often coma and death.

A much safer approach in the treatment of congestive heart failure would be the following: If the patient has been given average digitalizing and maintenance doses and does poorly, I consider this a presumptive sign, until proven otherwise, that either the dietary control is poor, or diuretic therapy is inadequate, or the patient's physical activity has not been curtailed sufficiently, or *the cause of the failure has not been recognized* It should, of course, be mentioned that a patient in failure may have reached such a state of cardiac dilatation that therapy of any kind is of little value, and death will occur regardless of what is done.

In short, digitalis should be considered only one of the measures used in the treatment of heart failure.

Contraindications to Digitalis.—The use and limitations of digitalis therapy in the treatment of congestive heart failure were described on page 218.

Digitalis should not be used prophylactically, even preoperatively, in a patient with organic heart disease, if no signs of heart failure have ever been present. *Similarly, digitalis should not be given to patients to control a sinus tachycardia due to any cause other than congestive heart failure,* notwithstanding the fact that digitalis is effective in abolishing attacks of paroxysmal tachycardia

The presence of acute myocardial infarction, angina pectoris, glomerular nephritis, bundle branch block, incomplete or even complete *a–v* block are not contraindications to the use of digitalis, if congestive heart failure is present. In fact, I have observed instances where complete *a–v* block disappeared in a patient with congestive heart failure when compensation was restored. Similarly, although premature auricular and ventricular contractions may result from digitalis toxicity, digitalis may cause these arrhythmias to disappear (even if the patient does not have congestive heart failure).

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Digitalis can also cause *sinus arrest, and various degrees of a–v* block. The most common is a prolonged *P–R* interval, but the Wenckebach type

of incomplete *a–v* block or a 2:1, 3:1, *etc.* *a–v* block are common, and even complete *a–v* block may occur. Occasionally nodal rhythm, sinus arrhythmia, or a wandering pacemaker are produced by digitalis.

Changes in the *RS–T* segment and *T* wave due to digitalis are usually considered physiological. However, I believe that when the direction of *T* is reversed, and *T* is fused with the *RS–T* segment which is markedly deviated, this is a sign of toxicity.

Other Toxic Manifestations.—Allergic rashes and even eosinophilia have been reported after digitalis.

Gynecomastia has also been reported from digitalis.

There is no level of dosage at which toxicity appears or fails to appear, because not only do the various preparations differ in potency, rate of absorption, and rate of dissipation, but there are marked individual variations in patients. Marked diuresis due to mercurial or other diuretics may indirectly produce digitalis toxicity. The reason for this is that the mercurials cause large quantities of potassium to be eliminated in the urine. The hypopotassemia which results sensitizes the heart to the action of digitalis and results in digitalis toxicity.

Treatment of Digitalis Toxicity.—First the digitalis must be stopped for an adequate period of time, until dissipation and excretion occurs. This may take two weeks or longer if one of the slowly acting preparations, such as digitalis leaf or digitoxin has been prescribed.

Ventricular premature contractions or ventricular tachycardia may respond to the oral administration of 5 to 10 grams of the potassium salts. (10 to 20 cc. of a 50 per cent solution of potassium chloride can be given in one dose orally.) If the patient is comatose, the solution can be introduced rectally, or 1 gram of potassium chloride can be given intravenously (10 cc. of a 10 per cent solution, given slowly at the rate of 1 cc. a minute).

Ventricular premature contractions or ventricular tachycardia may respond to the oral administration of 5 grams of potassium salts. This can be repeated in several hours if necessary. If the patient is comatose, a 25 per cent solution of potassium chloride in water can be introduced rectally or the potassium can be given intravenously. (See page 717 for more details on the administration of potassium salts.)

Paroxysmal tachycardia due to digitalis may also respond to magnesium sulfate intravenously (page 348) or procaine amide (page 353) even if the potassium salts are not effective.

For nausea and vomiting, cocaine, 30 mg. ($\frac{1}{2}$ grain), with 0.5 gram ($7\frac{1}{2}$ grains) of bismuth subcarbonate, can be given orally, several times a day. A new drug, *thorazine* (chlorpromazine hydrochloride) apparently is also very efficacious in stopping the vomiting due to digitalis intoxication. The dose is from 25 mg. to 150 mg. daily. (It is marketed in 10 mg. and 25 mg. tablets.)

When the vomiting is persistent, marked dehydration may develop. This must be energetically treated, and I have given as much as 4000 cc. of fluid parenterally in twenty-four hours. Of this quantity, not more than 1000 cc. should be isotonic saline. The remainder should be 5 or 10 per cent glucose in distilled water. The solution can be given intravenously or subcutaneously.

Toxic auricular fibrillation from digitalis has been treated successfully by the intravenous injection of 2 to 3 mg. of atropine.

Other Therapeutic Measures.—**Thoracentesis.**—Moderate pleural effusions need not be tapped, and will slowly be reabsorbed, but if flatness extends above the angle of the scapula posteriorly, and if orthopnea is present, the fluid should be removed

The best site for tapping the pleura is in the seventh intercostal space, at a point midway between the anterior and posterior axillary lines The seventh intercostal space can be easily identified by its relation to the angle of the scapula—when the arm is by the side of the body, this space is slightly overlapped by the angle

The patient is propped in a sitting position, with the arm elevated, and the skin cleansed with an antiseptic solution The skin and subcutaneous tissue is then infiltrated with a 1 per cent novocain solution, the pleura is then penetrated with an 18 gauge, 1½" or 2" needle, connected by means of a three-way stopcock to a 50 cc syringe The needle should be introduced as near as possible to the upper level of the rib, to avoid the intercostal artery. If a three-way stopcock is not used, one should avoid the entrance of air into the pleural space during inspiration by placing the gloved finger over the needle while the syringe is being emptied Not more than 1000 cc. of fluid should be removed at one sitting, and the procedure should be immediately stopped if dyspnea or cough increase, because of the possibility of acute pulmonary edema resulting from the paracentesis. After the needle is withdrawn, a small sterile dressing is placed over the puncture point

Abdominal Paracentesis—Ascites of cardiac origin usually responds to a low-sodium diet and mercurials, but if the patient is very orthopneic, the abdomen may be tapped. The patient urinates and then is placed in a sitting position, and the skin cleansed The point of puncture is about 1½ to 2" below the umbilicus, in the midline This area should first be percussed before making the puncture, and a flat note elicited (A tympanitic note would indicate that intestine lies beneath) The skin is anesthetized with novocain, and a small nick is then made with a scalpel so that trocar can be inserted without using undue force After the abdomen is entered, the trocar is withdrawn, leaving the cannula in place The fluid should gush out. If this does not happen, the cannula should be rotated or pushed in further The flow should be stopped for a few minutes from time to time to prevent too rapid abdominal decompression, because acute pulmonary edema can occur When the cannula is withdrawn, the skin opening is closed with a suture and a dry dressing placed over the wound

Venesection.—This has been discussed on page 237.

Mechanical Removal of Edema Fluid—Marked edema of the lower extremities can be drained off by making a one-inch incision on the dorsum of each foot, and having the patient propped up, with the legs dependent for the next forty-eight hours Massive quantities of fluid will drain from the incisions even for weeks. The incisions should be covered with sterile gauze. If the skin edge becomes irritated, it can be protected with vaseline gauze or cod liver oil ointment. Multiple needle punctures of the skin of the calves has also been recommended for this purpose An even more effective way of removing the edema fluid mechanically is with Southey's tubes These are small perforated cannulæ which are inserted into the legs or feet,

of incomplete a-v block or a 2:1, 3:1, *etc* a-v block are common, and even complete a-v block may occur. Occasionally nodal rhythm, sinus arrhythmia, or a wandering pacemaker are produced by digitalis.

Changes in the *RS-T* segment and *T* wave due to digitalis are usually considered physiological However, I believe that when the direction of *T* is reversed, and *T* is fused with the *RS-T* segment which is markedly deviated, this is a sign of toxicity

Other Toxic Manifestations.—Allergic rashes and even eosinophilia have been reported after digitalis

Gynecomastia has also been reported from digitalis.

There is no level of dosage at which toxicity appears or fails to appear, because not only do the various preparations differ in potency, rate of absorption, and rate of dissipation, but there are marked individual variations in patients. Marked diuresis due to mercurial or other diuretics may indirectly produce digitalis toxicity. The reason for this is that the mercurials cause large quantities of potassium to be eliminated in the urine The hypopotassemia which results sensitizes the heart to the action of digitalis and results in digitalis toxicity.

Treatment of Digitalis Toxicity —First the digitalis must be stopped for an adequate period of time, until dissipation and excretion occurs. This may take two weeks or longer if one of the slowly acting preparations, such as digitalis leaf or digitoxin has been prescribed.

Ventricular premature contractions or ventricular tachycardia may respond to the oral administration of 5 to 10 grams of the potassium salts. (10 to 20 cc of a 50 per cent solution of potassium chloride can be given in one dose orally) If the patient is comatose, the solution can be introduced rectally, or 1 gram of potassium chloride can be given intravenously (10 cc. of a 10 per cent solution, given slowly at the rate of 1 cc. a minute)

Ventricular premature contractions or ventricular tachycardia may respond to the oral administration of 5 grams of potassium salts. This can be repeated in several hours if necessary. If the patient is comatose, a 25 per cent solution of potassium chloride in water can be introduced rectally or the potassium can be given intravenously. (See page 717 for more details on the administration of potassium salts)

Paroxysmal tachycardia due to digitalis may also respond to magnesium sulfate intravenously (page 348) or procaine amide (page 353) even if the potassium salts are not effective

For nausea and vomiting, cocaine, 30 mg. ($\frac{1}{2}$ grain), with 0 5 gram ($7\frac{1}{2}$ grains) of bismuth subcarbonate, can be given orally, several times a day. A new drug, *thorazine* (chlorpromazine hydrochloride) apparently is also very efficacious in stopping the vomiting due to digitalis intoxication. The dose is from 25 mg. to 150 mg. daily. (It is marketed in 10 mg. and 25 mg. tablets.)

When the vomiting is persistent, marked dehydration may develop. This must be energetically treated, and I have given as much as 4000 cc. of fluid parenterally in twenty-four hours. Of this quantity, not more than 1000 cc. should be isotonic saline. The remainder should be 5 or 10 per cent glucose in distilled water The solution can be given intravenously or subcutaneously.

Toxic auricular fibrillation from digitalis has been treated successfully by the intravenous injection of 2 to 3 mg. of atropine.

Other Therapeutic Measures.—Thoracentesis.—Moderate pleural effusions need not be tapped, and will slowly be reabsorbed, but if flatness extends above the angle of the scapula posteriorly, and if orthopnea is present, the fluid should be removed

The best site for tapping the pleura is in the seventh intercostal space, at a point midway between the anterior and posterior axillary lines The seventh intercostal space can be easily identified by its relation to the angle of the scapula—when the arm is by the side of the body, this space is slightly overlapped by the angle

The patient is propped in a sitting position, with the arm elevated, and the skin cleansed with an antiseptic solution The skin and subcutaneous tissue is then infiltrated with a 1 per cent novocain solution, the pleura is then penetrated with an 18 gauge, 1½" or 2" needle, connected by means of a three-way stopcock to a 50 cc syringe The needle should be introduced as near as possible to the upper level of the rib, to avoid the intercostal artery. If a three-way stopcock is not used, one should avoid the entrance of air into the pleural space during inspiration by placing the gloved finger over the needle while the syringe is being emptied. Not more than 1000 cc. *of fluid should be removed at one sitting, and the procedure should be* immediately stopped if dyspnea or cough increase, because of the possibility of acute pulmonary edema resulting from the paracentesis After the needle is withdrawn, a small sterile dressing is placed over the puncture point.

Abdominal Paracentesis.—Ascites of cardiac origin usually responds to a low-sodium diet and mercurials, but if the patient is very orthopneic, the abdomen may be tapped. The patient urinates and then is placed in a sitting position, and the skin cleansed The point of puncture is about 1½ to 2" below the umbilicus, in the midline. This area should first be percussed before making the puncture, and a flat note elicited (A tympanitic note would indicate that intestine lies beneath) The skin is anesthetized with novocain, and a small nick is then made with a scalpel so that trocar can be inserted without using undue force After the abdomen is entered, the trocar is withdrawn, leaving the cannula in place. The fluid should gush out If this does not happen, the cannula should be rotated or pushed in further The flow should be stopped for a few minutes from time to time to prevent too rapid abdominal decompression, because acute pulmonary edema can occur. When the cannula is withdrawn, the skin opening is closed with a suture and a dry dressing placed over the wound

Venesection.—This has been discussed on page 237.

Mechanical Removal of Edema Fluid—Marked edema of the lower extremities can be drained off by making a one-inch incision on the dorsum of each foot, and having the patient propped up, with the legs dependent for the next forty-eight hours Massive quantities of fluid will drain from the incisions even for weeks. The incisions should be covered with sterile gauze If the skin edge becomes irritated, it can be protected with vaseline gauze or cod liver oil ointment Multiple needle punctures of the skin of the calves has also been recommended for this purpose. An even more effective way of removing the edema fluid mechanically is with Southey's tubes These are small perforated cannulæ which are inserted into the legs or feet,

and even the scrotum, by means of a trocar. The fluid drains off into rubber tubing connected to the end of the cannula which can be left in place for two days. Danger of infection is slight.

Total Thyroidectomy, Radioiodine and Antithyroid Drugs.—Some years ago, total thyroidectomy was advocated for congestive heart failure in an attempt to depress the metabolic needs of the body. This has fallen into disrepute. Recently, radioiodine I^{131}, has been used with this same purpose. Propylthiouracil and other antithyroid compounds have also been used, with poor results.

Ion-Exchange Resins.—*Cations* are ions which carry a positive electrical charge. *Anions* carry a negative charge. An ion-exchanger is simply an insoluble material which can remove an ion from a surrounding solution, exchanging and liberating into the solution an equivalent amount of another ion of the same electrical charge. The ion-exchangers used in clinical medicine are synthetic resins.

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The amount of sodium (and other cations) which are removed depends on the potency and quantity of the ion exchanger, on the pH and on the amount of the cations in the ingested food. One hundred grams of resin may remove as much as 4 grams of salt, rarely as low as 1 gram. For this reason, the resins must be considered only as an adjunct method of treating heart failure.

One disadvantage of the cation exchange resins is that other cations besides sodium are removed from the body, particularly, potassium, calcium and magnesium. Thus, if the resin is used for a length of time, hypopotassemia, or hypocalcemia with tetany can develop. The newer resins contain potassium to counteract the tendency toward hypopotassemia. Excess of the resin can also cause hyponatremia.

Another danger of the ion exchange resins is that when strong cations such as sodium and potassium and calcium are removed and replaced by hydrogen, severe acidosis can develop. (Renal damage with the appearance of granular casts in the urine may also result.) Even if an ammonium exchange resin is used and ammonia replaces the sodium taken out of the body, the tendency toward acidosis persists because this ammonia is converted by the liver into urea.

Another disadvantage of the resins is that they are bulky and frequently cause gastrointestinal disturbances, especially constipation. However,

vomiting and occasionally diarrhea may develop. The constipation can be controlled by mild laxatives, such as methylcellulose A further complication of resin therapy is that the resins can remove thiamin, riboflavin, alkaloids such as atropine or quinidine, and oral antibiotics such as aureomycin and similar drugs and streptomycin

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Carbo-Resin (Lilly) —This is a mixture of potassium and hydrogen carboxylic cation resins plus a small quantity of an anionic resin exchanger This latter is added to reduce the tendency to acidosis which the cation exchangers can cause in patients with severe renal impairment In such cases, the kidneys are unable to counteract the hydrogen of the ion exchanger.

It is sold in packets containing 8 grams each, and in powder form in one-pound bottles

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An average dose is approximately 45 grams a day, given in three divided doses, at or before meals. Fifteen grams are equivalent to 2 tablespoonfuls.

The resins are administered orally in water, orange juice, or low-sodium milk. The resins can also be placed in cereals, mashed potatoes, Jell-O, ice cream or in any semi-solid food

The use of supplemental potassium salts to prevent hypopotassemia is not generally recommended However, the patient can be instructed to drink 2 large glasses of orange juice daily as a means of obtaining potassium in a natural form

The patient and his family should also be warned to recognize early signs of the low-salt syndrome, namely, loss of appetite, nausea, muscular weakness, apathy, or mental confusion (see page 270)

Blood analyses for potassium, sodium, chloride and carbon dioxide should be done periodically, depending on the patient's condition If renal disease is present, the analyses should be done weekly The carbon dioxide determination is particularly valuable as a guide to acidosis The chloride is a good guide to the serum sodium concentration

The resins, as I mentioned above, can be considered a supplemental means of treating heart failure In some cases, they will prove effective when the patient has become refractory to the mercurials They can be given in conjunction with digitalis, and with the mercurials They can be used instead of ammonium chloride to potentiate the action of the mercurials.

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Symptoms.—The patient complains of muscular symptoms such as weakness, cramps and twitchings; central nervous system symptoms such as apathy, drowsiness, confusion, psychosis or coma, gastrointestinal symptoms such as anorexia, nausea, vomiting, and abdominal cramps Thirst is usually absent after the full development of the syndrome, but may be marked early.

Signs—Physical examination will show a dry, wrinkled skin with a loss of elasticity. The tongue and mucous membranes are also dry There may be tachycardia, a small weak pulse, postural hypotension or syncope, and even vascular collapse. Oliguria or anuria may be present The temperature may be normal, subnormal or may progressively rise as the dehydration becomes more intense

Laboratory Tests (Table 6) —There is a reduced serum concentration of both sodium and chloride. Potassium may be normal or slightly increased. The bicarbonate (HCO_3) is reduced The blood urea nitrogen is very high and the hematocrit is elevated, due to the dehydration.

TABLE 6 —SOME SERUM ELECTROLYTE DISTURBANCES IN HEART FAILURE

	Sodium (*mEq/L*)	*Potassium* (*mEq/L*)	*Chloride* (*mEq/L*)	*CO_2* (*HCO_3* *mEq/L*)	*BUN* (*mg %*)	*Hematocrit* (*vol %*)
Normal	140	3 5—5	100	25	15	45
Low sodium syndrome	125	5 4	75	15	140	60
Low chloride syndrome	135	3	75	48	100	60
High chloride syndrome	142	4	120	10	140	60
Dilution syndrome	115	6	85	18	180	30

If serum sodium determinations cannot be done, a rough estimate of sodium concentration may be obtained by adding 12 to the sum of the concentrations of chloride and bicarbonate in milliequivalents per liter. For example, if the chloride concentration is 88 mEq per liter and the bicarbonate 20 mEq per liter, the sodium concentration is 88 plus 20 plus 12, or 120 mEq per liter The major exceptions to this rule occur in uremia, or in diabetic acidosis In these conditions, an increase of unmeasured acid (anion) reduces the bicarbonate concentration, without necessarily affecting sodium or chloride concentration

Treatment.—The treatment of the *low sodium syndrome* is difficult Theoretically, it has been suggested that a slow infusion of 200 to 300 cc of a 5 per cent sodium chloride daily for two or three days should relieve a true depletion of sodium (The serum sodium level should rise 5 to 10 mEq /liter) However, I have not been impressed by such therapy and have found that it usually aggravates the heart failure and may cause pulmonary edema and death. However, if the serum sodium level is very low (between 115 and 120 mEq per liter or less), or if there has been a rapid fall in sodium without a gain in weight, it may be helpful.

are bed-ridden for many months. This predisposes to venous thrombosis and embolization Thrombosis may occur in the veins of the lower or upper extremities Another cause of thrombosis in heart failure is sudden, excessive dehydration, due to the mercurial and other diuretics. This may even cause cerebral thrombosis

Because of the frequent occurrence of thrombo-embolic complications in chronic heart failure, it has been suggested that long-term anticoagulant therapy (page 618) be employed However, patients who have chronic heart failure are very sensitive to the action of anticoagulants and may develop prolonged prothrombin time values with small doses. This is particularly found in cases with severe passive congestion of the liver.

Cathartics.—*The use of one-half* an ounce of *magnesium sulfate nightly* or several times a week as a purge has been recommended to decrease edema However, such a practice may weaken the patient.

Tobacco.—Smoking may decrease the vital capacity, induce coughing, and even produce severe chest pain, all of which embarrass the circulation I therefore encourage my patients to discontinue smoking.

DEHYDRATION AND ELECTROLYTE DISTURBANCES IN HEART FAILURE

The long continued use of powerful diuretics may cause serious and even fatal electrolyte imbalances. The most common is the *low sodium syndrome*, due to an excessive loss of water (dehydration) along with an excessive loss of sodium and chloride ions. Another common syndrome is the *low chloride alkalosis syndrome*, due to dehydration with an excessive loss of chloride and cations In both these conditions, the patient's symptoms and the findings on physical examination are due to the dehydration and general loss of electrolytes. However, the etiology, laboratory findings and treatment differ greatly These and some of the other common electrolyte disturbances which occur in heart failure are discussed below.

The Low Sodium Syndrome (Low Salt Syndrome, Salt Depletion Syndrome, Hypochloremic Acidosis Syndrome).—This syndrome is the result of excessive loss of sodium chloride (salt) from the extracellular fluid. In *most cases, it is produced by prolonged treatment with the mercurial* diuretics, especially in patients who have had a marked dietary restriction of salt as well It is frequently seen during the summer months The patients usually give a history of *having become refractory to the mercurials.*

The low sodium syndrome can also occur in patients who have not received vigorous diuretic treatment. *In such cases, a marked loss of salt* occurs from vomiting, sweating or diarrhea. In addition, a low serum sodium can develop if large quantities of fluid are removed from the pleural or abdominal cavity.

Renal disease appears to be necessary for the low sodium syndrome to develop In these cases, the damaged kidneys have lost their ability to conserve base (cation) by manufacturing ammonia. *Normally, chloride* and other anions can be excreted as ammonium salts However, with renal impairment, ammonia is not available, and fixed base, particularly sodium,

must be used. As a result, the mercurial diuresis results in an excessive loss of sodium and other cations.

Symptoms.—The patient complains of muscular symptoms such as weakness, cramps and twitchings, central nervous system symptoms such as apathy, drowsiness, confusion, psychosis or coma, gastrointestinal symptoms such as anorexia, nausea, vomiting, and abdominal cramps. Thirst is usually absent after the full development of the syndrome, but may be marked early.

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Dilution syndrome	115	6	85	18	180	30

If serum sodium determinations cannot be done, a rough estimate of sodium concentration may be obtained by adding 12 to the sum of the concentrations of chloride and bicarbonate in milliequivalents per liter. For example, if the chloride concentration is 88 mEq. per liter and the bicarbonate 20 mEq. per liter, the sodium concentration is 88 plus 20 plus 12, or 120 mEq. per liter. The major exceptions to this rule occur in uremia, or in diabetic acidosis. In these conditions, an increase of unmeasured acid (anion) reduces the bicarbonate concentration, without necessarily affecting sodium or chloride concentration.

Treatment.—The treatment of the *low sodium syndrome* is difficult. Theoretically, it has been suggested that a slow infusion of 200 to 300 cc. of a 5 per cent sodium chloride daily for two or three days should relieve a true depletion of sodium. (The serum sodium level should rise 5 to 10 mEq./liter.) However, I have not been impressed by such therapy and have found that it usually aggravates the heart failure and may cause pulmonary edema and death. However, if the serum sodium level is very low (between 115 and 120 mEq. per liter or less), or if there has been a rapid fall in sodium without a gain in weight, it may be helpful.

are bed-ridden for many months. This predisposes to venous thrombosis and embolization. Thrombosis may occur in the veins of the lower or upper extremities. Another cause of thrombosis in heart failure is sudden, excessive dehydration, due to the mercurial and other diuretics. This may even cause cerebral thrombosis.

Because of the frequent occurrence of thrombo-embolic complications in chronic heart failure, it has been suggested that long-term anticoagulant therapy (page 618) be employed. However, patients who have chronic heart failure are very sensitive to the action of anticoagulants and may develop prolonged prothrombin time values with small doses. This is particularly found in cases with severe passive congestion of the liver.

Cathartics.—The use of one-half an ounce of magnesium sulfate nightly or several times a week as a purge has been recommended to decrease edema. However, such a practice may weaken the patient.

Tobacco.—Smoking may decrease the vital capacity, induce coughing, and even produce severe chest pain, all of which embarrass the circulation. I therefore encourage my patients to discontinue smoking.

DEHYDRATION AND ELECTROLYTE DISTURBANCES IN HEART FAILURE

The long continued use of powerful diuretics may cause serious and even fatal electrolyte imbalances. The most common is the *low sodium syndrome*, due to an excessive loss of water (dehydration) along with an excessive loss of sodium and chloride ions. Another common syndrome is the *low chloride alkalosis syndrome*, due to dehydration with an excessive loss of chloride and cations. In both these conditions, the patient's symptoms and the findings on physical examination are due to the dehydration and general loss of electrolytes. However, the etiology, laboratory findings and treatment differ greatly. These and some of the other common electrolyte disturbances which occur in heart failure are discussed below.

The Low Sodium Syndrome (Low Salt Syndrome, Salt Depletion Syndrome, Hypochloremic Acidosis Syndrome).—This syndrome is the result of excessive loss of sodium chloride (salt) from the extracellular fluid. In most cases, it is produced by prolonged treatment with the mercurial diuretics, especially in patients who have had a marked dietary restriction of salt as well. It is frequently seen during the summer months. The patients usually give a history of having become refractory to the mercurials.

The low sodium syndrome can also occur in patients who have not received vigorous diuretic treatment. In such cases, a marked loss of salt occurs from vomiting, sweating or diarrhea. In addition, a low serum sodium can develop if large quantities of fluid are removed from the pleural or abdominal cavity.

Renal disease appears to be necessary for the low sodium syndrome to develop. In these cases, the damaged kidneys have lost their ability to conserve base (cation) by manufacturing ammonia. Normally, chloride and other anions can be excreted as ammonium salts. However, with renal impairment, ammonia is not available, and fixed base, particularly sodium,

The dose is 20 cc. daily. The patient sips 5 cc. of the acid in a full glass of water, four times a day, through a glass tube, to protect the teeth This is equivalent in chloride content to about 3 grams of ammonium chloride

The duration of therapy depends on the degree of chloride depletion It may take several days to a week or more. The patient usually responds within two to three days

Potassium can be given orally or intravenously (page 717) Calcium gluconate (10 cc. of a 20 per cent solution) can be given slowly, intravenously, as often as necessary.

Differentiation of the Low Chloride Syndrome from Respiratory Acidosis – An elevated plasma bicarbonate concentration with a reciprocal reduction in chloride concentration may occur in cardiac patients in two different ways. The usual cause, as mentioned above, is a low chloride syndrome, due to excessive mercurial diuresis The situation is similar to that which occurs after prolonged vomiting of acid gastric juice or after excessive ingestion of sodium bicarbonate or any other absorbable alkali However, a similar electrolyte pattern may occur in emphysema and pulmonary fibrosis with reduced pulmonary ventilation, when there is a retention of carbon dioxide. This accumulates in the blood as carbonic acid and produces a high blood bicarbonate level and a reduction of the plasma chloride At the same time, the blood becomes more acid

The best method of differentiating these two conditions is clinical. If low chloride and high bicarbonate values occur in a patient who has received mercurials and who does not have significant pulmonary disease, one can assume that the electrolyte disturbances are due to a *low chloride syndrome*. However, in a patient with chronic pulmonary emphysema, pulmonary fibrosis or chronic cor pulmonale due to multiple pulmonary infarctions, the low chloride and high bicarbonate plasma levels would suggest a *respiratory acidosis*. (The use of the blood pH theoretically would be helpful in differentiating these two conditions, because it tends to be high in a *high chloride syndrome* and low in *respiratory acidosis* However, pH determination is difficult and it may be within normal in both conditions.)

Treatment of Respiratory Acidosis.—The treatment of respiratory acidosis is difficult, particularly since these patients are often refractory to the mercurials. The use of ammonium chloride is contraindicated because it tends to increase the acidosis However, the carbonic anhydrase inhibitors (page 255) may be of value in such cases of heart failure due to cor pulmonale because they cause the elimination of carbon dioxide

The High Chloride Syndrome (Hyperchloremic Acidosis Syndrome, Ammonium Chloride Poisoning) —The high chloride syndrome can occur as a result of excessive ammonium chloride administration, or from use of the cation exchange resins, or from the carbonic anhydrase inhibitors.

If ammonium chloride is given for only three or four days at a time, it merely produces a mild, asymptomatic acidosis. However, if it is given continuously for weeks at a time, particularly in patients who already have an acidosis due to renal disease, it can produce a severe high chloride acidosis The cation exchange resins produce an acidosis by exchanging the ammonium or hydrogen of the resin for sodium. If the patient has

One reason that infusion of hypertonic sodium chloride is not helpful in the low sodium syndrome is that the low serum sodium level may not indicate a true depletion of sodium, but, instead may merely be due to the fact that as dehydration and increasing heart failure have occurred, the sodium has moved from the blood stream into the tissue cells, replacing the potassium which has moved from the cells to the blood.

The treatment which I have found lifesaving on occasions is to give massive infusions of glucose in distilled water. I have used as much as 5 liters in a period of twenty-four hours Such cases may also benefit from potassium salts These can be given orally in a dose of 4 to 6 grams a day (sometimes as high as 10 grams a day), rarely intravenously (see page 717 for the treatment of hypopotassemia). Regardless of the treatment used, the prognosis is poor

The Low Chloride Syndrome (Hypochloremic Alkalosis Syndrome).—The symptoms and physical signs of the low chloride syndrome are identical to those of the low sodium syndrome. However, the etiology, laboratory findings and treatment are different

Etiology—The low chloride syndrome is due to excessive diuresis produced by the mercurials. The mercurials cause the elimination of more chloride than sodium, the difference between these two ions being made up by potassium or ammonium or both The excessive loss of chloride in the urine with either of the latter two ions produces the following laboratory findings.

Laboratory Tests (Table 6) —The serum chloride is low. This is accompanied by a rise in serum bicarbonate and an alkalosis. The serum sodium concentration remains normal, or may be slightly elevated, due to the dehydration The serum potassium may be normal or slightly decreased However, this may mask a true potassium deficit, because hemoconcentration is present. Serum calcium concentration is usually normal, but may be reduced.

Clinical Picture—The alkalosis is rarely severe enough to produce symptoms of itself. The most frequent clinical finding is that the patient has become unresponsive to further mercurial therapy. (This occurs when the chloride level falls below 86 mEq /liter.) If one continues to use the mercurials at this stage, the full syndrome may develop in from three to seven days The patient loses weight rapidly, and dehydration with its typical symptoms and signs, described under the low sodium syndrome, develops.

Even though the serum calcium is reduced, clinical tetany usually does not develop The tetany is prevented by the low serum potassium level. However, if fluid containing potassium, but not calcium, is given, tetany may develop

Treatment.—The *low chloride syndrome* is easily treated with ammonium chloride or hydrochloric acid.

Ammonium chloride in the form of uncoated tablets can be given orally in a daily dose of 6 to 8 grams. (Enteric coated tablets should *not* be used.) If the patient cannot tolerate it orally, 4 to 8 grams of ammonium chloride can be given in a 1 per cent solution, intravenously, no faster than 200 cc. an hour.

Dilute hydrochloric acid (U.S.P , 10 per cent) is a satisfactory substitute for the ammonium chloride This can be conveniently given by mouth.

The dose is 20 cc. daily. The patient sips 5 cc of the acid in a full glass of water, four times a day, through a glass tube, to protect the teeth This is equivalent in chloride content to about 3 grams of ammonium chloride

The duration of therapy depends on the degree of chloride depletion It may take several days to a week or more. The patient usually responds within two to three days.

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good renal function, the acidosis produced is mild. However, if renal impairment is present, the acidosis may be severe. The carbonic anhydrase inhibitors produce an acidosis which results from the increased renal excretion of the bicarbonate ion (page 255).

When a high chloride acidosis occurs, the patient develops stupor or coma and a Kussmaul type of hyperpnea. (This condition should always be suspected when a patient in heart failure develops stupor or coma.)

Laboratory Tests (Table 6) —The serum chloride is high, sodium and potassium normal, the plasma bicarbonate is very low, the urea nitrogen slightly increased and the hematocrit high.

Treatment —The ammonium chloride should be stopped immediately. This usually is sufficient if the patient does not have renal disease. However, if the patient is comatose, large quantities of alkaline sodium salts must be given intravenously One to 3 liters of isotonic sodium bicarbonate, or isotonic sodium lactate ($\frac{1}{6}$ molar) can be used The infusion should be given very slowly, with the head of the bed elevated and with equipment ready for rapid venesection, or with tourniquets at hand If the patient can take medication by mouth, the alkali should be given orally

Frequent determinations of serum bicarbonate, Cl, and BUN can be used as a guide to the amount of the alkali to be used.

The Dilution Syndrome.(Low Sodium Dilution Syndrome).—In the dilution syndrome, the serum sodium and chloride levels are low as in the low sodium syndrome However, dehydration is *not* present, and the hematocrit value is low (Table 6).

The dilution syndrome usually occurs in patients with very severe congestive heart failure who are retaining water abnormally because of infection, *under-digitalization* or *over-digitalization*, or *other unknown* stresses, which apparently stimulate the production of the antidiuretic hormone of the posterior pituitary

These patients show symptoms of lassitude, apathy, anorexia and nausea. In addition they have severe and progressive edema, despite the use of increasingly large amounts of the mercurial diuretics

The low sodium and chloride levels in these cases are therefore due, not so much to a loss of salt, but to a retention of water. Apparently, when the heart failure becomes severe and renal blood flow diminishes to the point where there is very little sodium being brought to the tubules for reabsorption, the tubules reabsorb water instead

Hyperpotassemia and uremia may also occur in association with the low sodium syndrome This is due to the fact that the poorly functioning kidneys are unable to excrete the potassium ion.

Treatment of the dilution syndrome is difficult Large doses of sodium chloride have been advocated, but here, as in the treatment of the low sodium syndrome, the salt may precipitate fatal pulmonary edema and should *not* be used. Venesection may be of value in this condition.

Hypopotassemia (Hypokalemia).—A marked loss of potassium can be suspected if apathy, drowsiness, muscular weakness or circulatory collapse occurs in a patient who has been receiving large doses of the mercurials and has not been eating. The diagnosis can be confirmed by typical electrocardiographic findings of hypopotassemia (page 205) or by a low

potassium level in the blood. The diagnosis and treatment of hypopotassemia are described on page 716

Hypocalcemia.—The blood calcium level is rarely below normal even when marked electrolyte disturbances are present. However, carpopedal spasm may occur in the morning, on arising, and tetany may be produced when the electrolyte imbalance is being treated with fluid containing potassium (page 272).

The hypocalcemia responds quickly to calcium gluconate intravenously (10 cc of a 20 per cent solution) or of calcium lactate orally (15 grams daily) or the use of a low-sodium milk, such as Lonalac

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Chapter 14

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Pathological Physiology.—The etiology of shock can be divided into the following types.

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a, in acute hemorrhage, external or internal It is immaterial whether the hemorrhage is due to trauma or some medical condition such as a bleeding peptic ulcer, *etc*

b, with plasma loss, as in burns,

c, by loss of electrolytes, especially salt and water, as in severe diarrheas, continuous vomiting, Addison's disease, *etc.*

d, I have seen several cases of severe shock produced by hyaluronidase given to promote a rapid clysis of 5 or 10 per cent dextrose in distilled water. In such cases, the fluid was not absorbed into the blood stream as fast as it entered the subcutaneous tissues Instead, electrolytes and body fluids entered the clysis area, in an attempt to make the clysis fluid isotonic. This caused a sharp decrease in cardiac output and shock

2 **Failure of the Heart to Pump Because of Muscular Weakness of the Heart (Cardiogenic Shock).**—The circulating blood volume is normal in this form of shock, as it is in the remaining forms Cardiogenic shock may occur in several conditions·

a, in acute *myocardial infarction. Here, there is a sudden failure of the* left ventricle. If the right ventricle does not fail to the same degree, blood continues to be pumped into the lungs, and pulmonary engorgement may occur, even with shock.

Recent studies of shock produced by acute myocardial infarction have shown that the first change which occurs is a reduction of the stroke volume of the heart, due to the myocardial injury. This is followed by a series of compensatory mechanisms characterized by generalized, intense vasoconstriction, including constriction of the venous side of the vascular system, and by tachycardia, producing the shock-like picture

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As a result, the cardiac output is decreased, the venous pressure is raised, the circulation time is prolonged. However, the total blood volume remains unchanged, or is reduced only slightly.

If a paroxysmal tachycardia occurs, this will decrease the cardiac output still further and accentuate the shock. Also, if pulmonary edema occurs as a result of the myocardial infarct, the passage of large quantities of plasma from the blood stream into the lungs also decreases the cardiac output and aggravates shock. Another factor which may increase the shock is that some cardiac patients develop a marked hypotension when given morphine.

b, in paroxysmal tachycardia, the very rapid rate prevents adequate diastolic filling.

c, in the terminal stages of congestive heart failure, shock may also occur.

3 **Inability of the Heart to Fill, Due to Increased Intrapericardial Pressure.**—This occurs in acute pericardial tamponade, which may be due to trauma, infection, *etc.* The increased intrapericardial pressure prevents the return of blood to the heart.

4 **Obstruction of the Main Arterial Pathways, as in Massive Pulmonary Embolism**

5 **Loss of Vasomotor Tone.**—This occurs in primary shock, in fainting, in reactions to nitrites, *etc.* However, it may be an important accessory factor even in cases of secondary shock, as for example, in the case of a young man suffering from shock due to a laceration of the scalp which had bled profusely. He was conscious and with a fairly good pulse volume. An attendant sat the patient up, but he immediately became pale, pulseless, lost consciousness and expired in a few minutes.

6 **Widespread Failure of Cell Metabolism as in Acute Infections.**—This also occurs if shock is unduly severe or greatly prolonged, and probably is the cause of so-called irreversible shock.

The cause of so-called *irreversible shock* has been carefully studied recently. It has been found that in several forms of experimental shock there first occurs a hyper-reactive, vasoconstrictor state. This is caused by a vasoexcitor principle, *VEM*, which is formed in the anoxic kidneys. At this time, a vasodilator principle, *VDM*, is also being formed by the anoxic liver, but at this stage, it is also inactivated by the liver. Later, during the stage of profound irreversible shock, the anoxic liver no longer inactivates *VDM*, which then appears in the blood in increasing amounts.

It has therefore been assumed that the presence of *VDM* in the blood is the cause of irreversible shock. Although this has not been confirmed, animal experiments have shown that the liver plays a part in the mechanism of irreversible shock. Dogs, for example, normally harbor intestinal bacteria, particularly Clostridia, in their livers. During shock these bacteria grow rapidly. However, if the animals have been pretreated with aureomycin or some other similar antibiotic which is effective against the Clostridia, they are able to survive an otherwise fatal bleeding. These observations also show the importance of infection as a cause of irreversible shock.

In any one case, multiple factors may be present. In addition, regardless of the cause of shock, selective vasoconstriction occurs in various parts of the body in an attempt to counteract the decreased cardiac output. This

is particularly marked in the kidneys where the blood flow may decrease even to one-tenth or one-twentieth or less.

Symptoms and Signs.—The acute onset of shock with pallor, cold, moist, *clammy extremities, skin which has an ashen-gray or cyanotic tint, thready* pulse of poor quality, and the drop in systolic blood pressure to about 90 mm or less is very dramatic The patient usually does not lose consciousness He lies quietly, listless and apathetic, but may be restless and apprehensive, or at times, confused and even manic. Nausea, vomiting and great thirst may appear The temperature is usually subnormal, but in cases of acute infections or acute myocardial infarction, the rectal temperature may be elevated If the skin is very cold, the low temperature may prevent reduction of hemoglobin, and cold, red, blotchy areas appear instead of cyanosis

The venous pressure may be normal, but it is usually subnormal and the veins of the extremities are collapsed. However, in cases of heart failure, acute pericardial tamponade or pulmonary embolism, the pressure in the neck veins may be elevated

Other variations from the classical picture that may be encountered are a warm skin, even though the blood pressure may fall, or a slow pulse, and rarely maintenance of blood pressure even though the other signs of shock are present.

Recently, six different circulatory patterns of shock have been described (Grant and Reeve):

1 Cold tachycardia with a normal blood pressure, fast pulse, cold *extremities and pale face* This has been *encountered only after injury*, associated with moderate blood loss

2 Warm tachycardia, with a normal blood pressure, fast bounding pulse, warm extremities and well colored face This has been found with 70 per cent blood volume, or in patients with a very low hemoglobin

3 Hypertensive pattern, with only a slight decrease in blood pressure This has been encountered soon after injury.

4 Vasovagal pattern, with a low blood pressure, slow pulse, cold extremities and pale face This is usually seen early, with emotional disturbances, and occasionally as a terminal event in patients dying of hemorrhage (It is actually a form of syncope, page 287)

5. Cold hypotension, with a low blood pressure, fast pulse, cold extremities and pale face This is seen in advanced shock with severe blood loss It also occurs in advanced sepsis

6 Warm hypotension, with a low blood pressure, fast pulse, warm extremities This is usually a transient condition with moderate blood loss, *encountered in warm surroundings, often after operation.*

Course and Prognosis.—Shock is a serious complication, and frequently results in death Why some patients recover quickly from shock, and why, in others, even intensive therapy is unsuccessful, is difficult to answer, and is probably related to the depth and duration of the shock, and the presence of accessory factors, such as infection, loss of vasomotor control, *etc*

Shock may also produce acute renal failure (acute tubular necrosis, lower nephron syndrome) with oliguria, proteinuria, casts, cells and debris in the urine and progressive uremia, which may cause death in a week or so, even though the general circulation has already returned to normal

As a result, the cardiac output is decreased, the venous pressure is raised, the circulation time is prolonged. However, the total blood volume remains unchanged, or is reduced only slightly.

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In any one case, multiple factors may be present. In addition, regardless of the cause of shock, selective vasoconstriction occurs in various parts of the body in an attempt to counteract the decreased cardiac output. This

average maintenance dose ranges from 0.5 to 1 cc. (2 to 4 micrograms of base) per minute.

If the patient requires large quantities of fluid in addition to the norepinephrine, a more dilute solution can be used. However, if large quantities of fluid are not desirable, a greater concentration can be used.

Mephentermine sulfate (*wyamine sulfate*) is supplied in vials of 1 cc. and 10 cc. Each 1 cc. contains 15 mg. of mephentermine sulfate. The drug can be given intramuscularly or intravenously.

In most cases, an initial intravenous dose of 15 mg. (1 cc.) can be given slowly over a period of one to two minutes. A pressor response should be noticed immediately. If this does not occur, a second injection of 15 to 30 mg. (1 to 2 cc.) can be given immediately after the first. The dose can then be repeated every thirty to forty-five minutes, when the effect of the drug becomes dissipated.

After the blood pressure has risen to approximately 120 mm. Hg, it can be maintained in three ways.

1. Repeated doses of the concentrated mephentermine intravenously, every thirty to forty-five minutes, as its effect is dissipated.

2. A continuous intravenous drip. Thirty milligrams (2 cc.) of the drug are added to 100 cc. of 5 per cent glucose in distilled water. The rate of flow should be approximately 15 drops per minute. However, the rate of flow should be adjusted to maintain a desired blood pressure.

3. Intramuscularly in doses of 15 to 30 mg. (1 to 2 cc.). A rise in blood pressure will occur within five to fifteen minutes after the intramuscular injection and will persist for one to two hours.

Occasionally, one intravenous injection is sufficient to raise and maintain the blood pressure at a satisfactory level.

D-desoxyephedrine (*desoxyn, methedrine*) is supplied in 1 cc. (20 mg.) ampoules. Ten to 20 mg. (0.5 to 1 cc.) can be given intravenously every half-hour until the blood pressure is raised and maintained at a desired level.

These procedures may cause the blood pressure to rise to a hypertensive level, and pulmonary edema and death may occur. In addition, local reactions may occur at the site of injection, due to the intense vasoconstriction which the drugs cause. Tissue necrosis and ulceration of the skin due to extravasation of norepinephrine and neosynephrine, have been reported. In addition, a phlebitis may develop in the vein used for the injection. These complications are less likely to develop if the injection is made in the veins of the upper extremity.

B. *Transfusion.*—Five hundred to 1000 cc. or more of whole blood or plasma may also be effective in combatting the shock of myocardial infarction.

Rapid intra-arterial transfusion has also been used recently in shock. However, it has been shown that it is not any more effective than rapid intravenous transfusion of blood or plasma. In addition, gangrene may occur from intra-arterial transfusion, especially if the radial artery is used.

C. *Digitalization.*—I have seen patients in shock due to acute myocardial infarction, whose clinical condition strongly resembled that of acute heart failure, especially right-sided heart failure, with engorgement of the liver and an elevated venous pressure. Rales were not always present.

Treatment.—The treatment of shock should be prompt and directed at the etiology So-called surgical shock is easily treated with blood or plasma The treatment of shock in medical and cardiac conditions is more difficult. With pericardial tamponade, paracentesis may be lifesaving

A description of the treatment of medical shock, with emphasis on the shock due to myocardial infarction, is as follows:

When shock occurs after myocardial infarction, an apparently irreversible state often occurs after several hours. For this reason it is important to recognize the presence of shock in a patient who has a myocardial infarct and to institute treatment promptly.

Shock can be considered to be present when the systolic blood pressure falls abruptly and remains below an arbitrary level of 80 mm Hg for an hour or more (In a patient who previously has had hypertension, shock may occur at a higher pressure of 90 or 100 mm. Hg) During this time, the characteristic clinical picture of shock appears with a rapid pulse, small pulse pressure, poor heart sounds, gallop rhythm, gray, sickly cyanosis, weakness, faintness, cold, moist skin, stupor or coma (Also see above).

Several forms of treatment are available:

A *Vasopressor Drugs* —Vasopressor amines such as neosynephrine (phenylephrine), d-desoxyephedrine hydrochloride (methedrine, desoxyn), norepinephrine (arterenol, levophed), mephentermine (wyamine), and other amines have been used successfully to combat the shock resulting from acute myocardial infarction. These drugs cause a marked vasoconstriction, increase the venous return to the heart and thereby raise the cardiac output

Neosynephrine is supplied as a 0 2 per cent solution in ampoules of 2 cc Each 1 cc contains 2 mg (A 1 per cent solution is also available, but should not be used) The usual dose is 0.5 mg. (0.25 cc. of the 0.2 per cent solution), injected intravenously. This can be repeated until the blood pressure rises to about 120 mm. Hg.

Norepinephrine (levophed, arterenol) is supplied as the bitartrate salt in a 0 2 per cent solution (equivalent to 0 1 per cent of the base). Each ampoule contains 4 cc , and *must* be diluted in the following way for use:

Norepinephrine is administered in 5 per cent dextrose in distilled water or normal saline It should not be administered in saline solution alone. Whole blood or plasma can be given simultaneously if needed to increase the blood volume However, if this is done, it should be administered separately, by using a Y-tube and individual flasks

The contents of one 4 cc. ampoule of norepinephrine is added to 1000 cc. of 5 per cent dextrose solution. (Each 1 cc. of this dilution contains 4 micrograms of norepinephrine base This is equivalent to 8 micrograms of the bitartrate).

This dilution is given intravenously, using a needle or polyethylene tubing, well advanced into the vein and securely fixed, through a drip bulb which allows an accurate estimation of the rate of flow in drops per minute. After observing the response to an initial dose of from 2 to 3 cc. (from 8 to 12 micrograms of base) per minute, the rate of flow should be adjusted to produce and maintain the desired level of blood pressure. The

Chapter 15

SYNCOPE AND RELATED STATES

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Study of the blood pressure and pulse while these phenomena are developing show that at first the systolic pressure falls and the heart rate increases, but the diastolic pressure remains unchanged or even rises slightly. However, just prior to syncope there is a precipitous fall in both the systolic and diastolic pressures and a slowing of the heart rate. The bradycardia that develops is secondary because it can be prevented by atropine without preventing the development of syncope.

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In such cases, rapid digitalization with lanatoside C (page 258) has occasionally proved lifesaving.

To conclude, the presence of shock in a case of acute myocardial infarction is a serious sign and requires urgent treatment. My own preference is for the vasopressor drugs rather than transfusion. However, we do not yet have an ideal treatment for shock and many patients will die of it even in spite of heroic treatment.

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Syncope can also occur after exertion in cases of cor pulmonale and in the tetralogy of Fallot In the tetralogy of Fallot, it is due to anoxemia produced by the entrance of large quantities of unoxygenated blood from the muscles In cor pulmonale, exercise requires an increased cardiac output, but the weak right ventricle is unable to increase its output sufficiently.

HYPERACTIVE CAROTID SINUS REFLEX

The carotid sinus is a small bulbous dilatation normally present at the bifurcation of the common carotid artery. It is richly supplied with sensory receptor fibers which are connected to a delicate sinus nerve which runs upward between the internal and external carotid arteries to join the glossopharyngeal nerve, finally connecting with the vasomotor and cardioinhibitor centers of the medulla. The carotid sinus responds to changes in pressure within the carotid artery. Compression of the carotid artery at its bifurcation produces a rise in pressure within the sinus, thus causing a slowing of the heart rate, a fall in blood pressure and peripheral vasodilatation On the other hand, pressure on the common carotid artery a distance below the carotid sinus may reduce the pressure within the sinus and thus cause an increase in heart rate, a rise in blood pressure and vasoconstriction.

In certain persons the carotid sinus may become abnormally hyperactive or sensitive, and cause syncope and related symptoms. The following three types of carotid sinus sensitivity have been described:

1 **The Vagal Type of Carotid Sinus Sensitivity.**—The symptoms are due to reflex vagal inhibition of the heart, causing a marked slowing of the heart, or asystole, and a secondary fall in blood pressure.

2 **The Vasomotor Depressor Type of Carotid Sinus Sensitivity.**—The attack follows a direct reflex fall of blood pressure, independent of any change in heart rate. The fall of blood pressure is due to reflex vasodilatation.

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Symptoms and other clinical manifestations of carotid sinus sensitivity may occur spontaneously, or can be induced by mechanical stimulation of the sinus by means of digital pressure, in the following way:

Testing the Carotid Sinus Reflex.—The carotid sinus can be located anterior to the sternomastoid muscle at the upper level of the thyroid cartilage (Adam's apple), and sometimes one-half inch above it. In applying pressure over the carotid sinus, the examiner stands behind the patient, who should be lying, and, with two fingers, presses the artery against the transverse process of the sixth cervical vertebra The pulsating artery should be felt under the finger tips, and pressure should be maintained for fifteen to twenty seconds. Simultaneously, the area should be massaged by the pressing fingers A more marked response is often obtained on the right side than on the left side

Normally, the heart usually slows less than 6 beats per minute, or the blood pressure falls less than 10 mm. of mercury. In a sensitive person, pressure on the sinus will produce the attack within fifteen or twenty

seconds, and in cases of the cerebral type, syncope may occur within three or four seconds after the sinus has been stimulated When slowing of the heart occurs, it is usually due to sinus bradycardia However, other arrhythmias, such as sinus arrest, incomplete or complete a–v block, nodal rhythm or even a short run of ventricular fibrillation may occur

An aura may precede the loss of consciousness There may be visual hallucinations, a sense of epigastric or substernal discomfort, or ringing in the ears, and then unconsciousness which may even be followed by convulsive movements

Digital stimulation of the carotid sinus is safe in young persons, but in elderly patients, monoplegia or hemiplegia can develop immediately after carotid sinus stimulation

Spontaneous Attacks.—Spontaneous attacks can be precipitated by sudden turning of the head to the side or upwards, by standing or other sudden changes in position, on wearing a tight collar, on emotional excitement, or occasionally in association with a tumor of the carotid body

The attacks vary in frequency and intensity In women, there is a tendency for attacks to recur at the time of menstruation The attacks usually occur on sitting or standing They usually last from a half a minute to three minutes, but if of the cerebral type, may last longer Recovery is rapid with only occasional after-complaints of headache

Patients with the vagal or vasomotor depressor type of carotid sinus sensitivity are often elderly, or have coronary atherosclerosis, or hypertension. However, biliary tract disease, esophageal diverticula, and other noncardiac conditions may also sensitize the carotid sinus Similarly, digitalis can sensitize the carotid sinus, especially in an elderly patient

Patients who suffer from the cerebral type of carotid sinus sensitivity are usually younger than those who suffer from the first two types, and often show signs of an unstable autonomic nervous system with palpitation, hot flushes, and emotional instability, moist palms and soles, marked daily fluctuations in blood pressure, dermographism, acrocyanosis and urticaria

Diagnosis.—The attacks can be reproduced by mechanical stimulation of the carotid sinus using digital pressure

Course and Prognosis—The condition is self-limited, but if the attacks occur frequently, they may seriously incapacitate the patient

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The vagal type of sensitivity can be prevented with atropine, 0.33 mg ($\frac{1}{200}$ grain) orally, or Tr Belladonnae, 10 minims, several times a day Ephedrine hydrochloride or sulfate, 8 mg ($\frac{1}{8}$ grain), orally, or other pressor drugs such as paredrine hydrobromide, 20 mg orally, several times daily are helpful in both the vagal and in the vasomotor depressor type of sensitivity which will not respond to atropine. The cerebral type does not respond to any of these drugs, but may respond to sedatives

Recently, the atropine-like drug, *pro-banthine*, in a dose of 15 mg (1 tablet), three or four times a day, has been found helpful

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2. **The Vasomotor Depressor Type of Carotid Sinus Sensitivity.**—The attack follows a direct reflex fall of blood pressure, independent of any change in heart rate. The fall of blood pressure is due to reflex vasodilatation.

3. **The Cerebral Type of Carotid Sinus Sensitivity.**—Prompt unconsciousness occurs without slowing of the heart or a fall of blood pressure.

Symptoms and other clinical manifestations of carotid sinus sensitivity may occur spontaneously, or can be induced by mechanical stimulation of the sinus by means of digital pressure, in the following way:

Testing the Carotid Sinus Reflex.—The carotid sinus can be located anterior to the sternomastoid muscle at the upper level of the thyroid cartilage (Adam's apple), and sometimes one-half inch above it. In applying pressure over the carotid sinus, the examiner stands behind the patient, who should be lying, and, with two fingers, presses the artery against the transverse process of the sixth cervical vertebra. The pulsating artery should be felt under the finger tips, and pressure should be maintained for fifteen to twenty seconds. Simultaneously, the area should be massaged by the pressing fingers. A more marked response is often obtained on the right side than on the left side.

Normally, the heart usually slows less than 6 beats per minute, or the blood pressure falls less than 10 mm. of mercury. In a sensitive person, pressure on the sinus will produce the attack within fifteen or twenty

seconds, and in cases of the cerebral type, syncope may occur within three or four seconds after the sinus has been stimulated. When slowing of the heart occurs, it is usually due to sinus bradycardia However, other arrhythmias, such as sinus arrest, incomplete or complete *a-v* block, nodal rhythm or even a short run of ventricular fibrillation may occur.

An aura may precede the loss of consciousness. There may be visual *hallucinations, a sense of epigastric or substernal discomfort, or ringing in* the ears, and then unconsciousness which may even be followed by convulsive movements.

Digital stimulation of the carotid sinus is safe in young persons, but in elderly patients, monoplegia or hemiplegia can develop immediately after carotid sinus stimulation

Spontaneous Attacks.—Spontaneous attacks can be precipitated by sudden turning of the head to the side or upwards, by standing or other sudden changes in position, on wearing a tight collar, on emotional excitement, or occasionally in association with a tumor of the carotid body.

The attacks vary *in frequency and intensity. In women, there is a* tendency for attacks to recur at the time of menstruation. The attacks usually *occur on sitting or standing They usually last from a half a minute* to three minutes, but if of the cerebral type, may last longer Recovery is *rapid with only occasional after-complaints* of headache

Patients with the vagal or vasomotor depressor type of carotid sinus sensitivity are often elderly, or have coronary atherosclerosis, or hypertension However, biliary tract disease, esophageal diverticula, and other noncardiac conditions may also sensitize the carotid sinus Similarly, digitalis can sensitize the carotid sinus, especially in an elderly patient

Patients who suffer from the cerebral type of carotid sinus sensitivity *are usually younger than those who suffer from the first two types, and* often show signs of an unstable autonomic nervous system with palpitation, hot flushes, and emotional instability, moist palms and soles, marked daily fluctuations in blood pressure, dermographism, acrocyanosis and urticaria

Diagnosis.—The attacks can be reproduced by mechanical stimulation of the carotid sinus using digital pressure

Course and Prognosis.—The condition is self-limited, but if the attacks occur frequently, they may seriously incapacitate the patient.

Treatment.—The attacks *often occur on sitting* and standing and can be sometimes aborted if the patient lies down immediately The patient should not wear tight collars *Mild sedation can be prescribed to decrease the* sensitivity of the sinus

The vagal type of sensitivity can be prevented with atropine, 0 33 mg. ($\frac{1}{200}$ grain) orally, or Tr Belladonnæ, 10 minims, several times a day *Ephedrine hydrochloride or sulfate, 8 mg ($\frac{1}{8}$ grain), orally, or other pressor* drugs such as paredrine hydrobromide, 20 mg orally, several times daily *are helpful in both the vagal and in the vasomotor depressor type of sen*sitivity which will not respond to atropine The cerebral type does not *respond to any of these drugs,* but *may respond to sedatives*

Recently, the atropine-like drug, *pro-banthine*, in a dose of 15 mg (1 tablet), three or four times a day, has been found helpful

the nitrites, hyperventilation, hysteria and many other conditions can produce syncope.

Syncope can also occur after exertion in cases of cor pulmonale and in the tetralogy of Fallot. In the tetralogy of Fallot, it is due to anoxemia produced by the entrance of large quantities of unoxygenated blood from the muscles. In cor pulmonale, exercise requires an increased cardiac output, but the weak right ventricle is unable to increase its output sufficiently.

HYPERACTIVE CAROTID SINUS REFLEX

The carotid sinus is a small bulbous dilatation normally present at the bifurcation of the common carotid artery. It is richly supplied with sensory receptor fibers which are connected to a delicate sinus nerve which runs upward between the internal and external carotid arteries to join the glossopharyngeal nerve, finally connecting with the vasomotor and cardioinhibitory centers of the medulla. The carotid sinus responds to changes in pressure within the carotid artery. Compression of the carotid artery at its bifurcation produces a rise in pressure within the sinus, thus causing a slowing of the heart rate, a fall in blood pressure and peripheral vasodilatation. On the other hand, pressure on the common carotid artery a distance below the carotid sinus may reduce the pressure within the sinus and thus cause an increase in heart rate, a rise in blood pressure and vasoconstriction.

In certain persons the carotid sinus may become abnormally hyperactive or sensitive, and cause syncope and related symptoms. The following three types of carotid sinus sensitivity have been described:

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Normally, the heart usually slows less than 6 beats per minute, or the blood pressure falls less than 10 mm of mercury. In a sensitive person, pressure on the sinus will produce the attack within fifteen or twenty

2. Orthostatic Hypotension Due to Impaired or Absent Vasomotor Reflexes.—This type of orthostatic hypotension is comparatively rare. It was first described by Bradbury and Eggleston. On standing, both the systolic and diastolic pressures fall precipitously without any appreciable increase in the heart rate, even though syncope results Other associated abnormalities are often present, such as decreased sweating responses, either locally or generally, and organic disease of the central nervous system, such as tabes dorsalis, syringomyelia, hematomyelia, *etc.* It has also been reported in cases of Addison's disease and Simmond's disease and in diabetes mellitus The patient may have impotence, a moderate anemia and a blood urea value at the upper level or normal. The condition is worse in hot weather.

In some cases, there are widespread disturbances in vasomotor control, and periods of hypertension may alternate with those of normal blood pressure and postural hypotension In addition, the heart rate may increase on standing, due not to a compensatory sinus tachycardia, but to a paroxysmal auricular tachycardia. The electrocardiogram remains unchanged, even if syncope occurs

Course and Prognosis.—This depends on the condition responsible for the postural hypotension

Treatment.—This is generally unsatisfactory, and elastic bandages, an abdominal binder or pressor drugs are often useless The intramuscular administration of desoxycorticosterone acetate, 5 mg , several times weekly may be of value A head-up bed has also proven helpful The head posts should be elevated about 18 inches—they can be placed on kitchen chairs It may be necessary to place a hard pillow under the mattress at the level of the thighs to prevent the patient from slipping downward at night.

3 **Orthostatic Hypotension with Abnormal Vasomotor Reflexes and Abnormal Pooling of Blood.**—Orthostatic hypotension of this type is occasionally seen after sympathectomy for hypertension. There is a loss of vasoconstrictor control because of the sympathectomy. However, the accelerator nerves are left intact, so that a compensatory tachycardia occurs on standing

SUDDEN NATURAL DEATH

By sudden natural death is meant death which occurs instantly or within a few minutes, but is not due to trauma However, also included under the term of sudden natural death, are cases of an acute illness which are fatal within twenty-four hours

Common cardiovascular causes of sudden death are acute myocardial infarction with or without rupture of the ventricle, aneurisms of the aorta with rupture, dissecting aneurism of the aorta with rupture, syphilitic aortitis, coronary artery disease, massive pulmonary embolism, aortic stenosis, pericardial tamponade, acute myocarditis, congenital cardiovascular lesions, subarachnoid or cerebral hemorrhage, and cerebral thrombosis. Common noncardiac causes of sudden death are acute infections, especially pneumonia, and diseases of the digestive and respiratory tracts including massive internal hemorrhage, and perforation of a viscus. In some patients, there is no apparent explanation for the sudden death Death usually occurs from cardiac standstill, but fatal ventricular fibrillation may occur

Roentgen therapy to the carotid sinus may be beneficial in cases which do not respond medically. Surgical denervation of the carotid sinus is now rarely done

If the patient is seen during an attack, atropine, 1 mg. ($\frac{1}{60}$ grain), can be injected intravenously, or epinephrine, $\frac{1}{1000}$, can be injected subcutaneously in a dose of 0.5 cc

ORTHOSTATIC HYPOTENSION

When a normal person stands, pooling of blood occurs in the lower extremities, along with a sudden drop in blood pressure. The drop in blood pressure stimulates receptor endings in the carotid sinus, aortic arch and probably other centers, and peripheral vasoconstriction occurs with an increase in heart rate, so that the fall in systolic pressure is minimal, and the diastolic pressure may become slightly elevated. Elevation of the systolic pressure may also occur

In orthostatic (postural) hypotension, a marked fall in blood pressure occurs on standing. This is often accompanied by a feeling of marked weakness or dizziness, blurring of the vision, and even syncope, due to cerebral anoxia

There are three different types of orthostatic hypotension:

1 **Orthostatic Hypotension with Normal Vasomotor Reflexes.**—This is the common form of orthostatic hypotension. In such cases, on standing, a tachycardia appears, the systolic pressure drops and the diastolic pressure tends to become elevated, just as in a normal person. However, such marked pooling of blood occurs in the lower extremities that the venous return is deficient, and the cardiac output falls, resulting in syncope or a feeling of weakness or exhaustion on standing

This type of postural hypotension occurs in patients who have extensive varicose veins of the lower extremities, or an abnormally large venous capacity, due for example to an abnormality such as a venous angioma of the lower extremity. It is seen in patients recovering from febrile illnesses or those confined to bed for a long time, with a resultant loss of muscle tone. It has also been reported in association with myasthenia gravis, in pregnancy, anemias, and can be produced by nitrites, or even by strapping a normal person on a tilt table, inclined to an angle of 60°. It also occurs in athletes who stand still after violent exercise.

Marked postural changes may occur in the electrocardiogram of such cases. A marked sinus tachycardia occurs along with extensive changes in the *T* waves The *T* may become downward in all precordial leads, in leads *aVL*, *aVF* and II and III, and flat in lead *aVR* These changes disappear immediately on lying (Similar postural electrocardiographic changes may appear in persons who do not suffer from postural hypotension.)

Course and Prognosis.—The condition is self-limited, but if severe, may incapacitate the patient.

Treatment.—Measures that increase the venous return of the lower extremities, such as the use of elastic bandages or stockings or a tight abdominal binder, are helpful. In addition, pressor drugs, such as ephedrine or paredrine (see page 289 for dosage), are valuable. Benzedrine, 5 to 10 mg. several times a day has also been used.

2. **Orthostatic Hypotension Due to Impaired or Absent Vasomotor Reflexes.**—This type of orthostatic hypotension is comparatively rare It was first described by Bradbury and Eggleston On standing, both the systolic and diastolic pressures fall precipitously without any appreciable increase in the heart rate, even though syncope results Other associated abnormalities are often present, such as decreased sweating responses, either locally or generally, and organic disease of the central nervous system, such as tabes dorsalis, syringomyelia, hematomyelia, *etc.* It has also been reported in cases of Addison's disease and Simmond's disease and in diabetes mellitus The patient may have impotence, a moderate anemia and a blood urea value at the upper level or normal. The condition is worse in hot weather.

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Chapter 16

THE ANGINAL SYNDROME

ANGINA PECTORIS as described by Heberden in 1772, and by most cardiologists until about thirty years ago, also included cases of acute myocardial infarction. Inasmuch as the pathology, clinical picture, and treatment of the two conditions are different, they warrant separate descriptions. Thus, angina pectoris will be described in the following pages, and acute myocardial infarction in Chapter 38, page 588.

ANGINA PECTORIS

Angina pectoris, or stenocardia, can be described as a symptom-complex consisting of short bouts of paroxysmal substernal (retrosternal) and precordial oppression, with or without radiation, lasting from a few seconds to fifteen minutes, rarely longer, usually precipitated by exertion, due to myocardial anoxia, and relieved by vasodilators such as nitroglycerin, or by momentary rest.

Pathological Physiology.—Angina pectoris is produced by transient myocardial anoxia, or coronary insufficiency as it is often called. Myocardia anoxia occurs when there is a disproportion between the oxygen requirements of the heart and the coronary blood flow. Thus myocardial anoxia can be produced by: *A*, decreased coronary blood flow; *B*, increased oxygen requirements of the heart muscle; or, *C*, a combination of both factors.

A. Decreased Coronary Blood Flow.—This can be produced in several ways:

1. By actual occlusion of one or more of the major coronary arteries. This does not necessarily lead to myocardial infarction if the process of occlusion is sufficiently slow for collateral circulation to develop. The collateral vessels that form can communicate between the arteries and the cavity of the heart, or between capillaries, the Thebesian veins and the cavity of the heart, or even between two major arteries.

2. Spasm of a relatively normal, or arteriosclerotic coronary artery may occur for a few minutes.

3. Deficient blood flow through the coronary arteries even though they remain patent. This can occur in cases of syphilitic aortic insufficiency where the mouths of the coronary arteries are also involved in the inflammatory process (the coronary arteries originate in the sinuses of Valsalva, just above the cusps of the aortic valve), or in cases of calcific aortic stenosis where calcification of the mouths of the coronary arteries may also occur. Deficient blood flow through the coronary arteries can also occur in the absence of pathology of the vessels as in a case of rheumatic, or even syphi-

litic aortic insufficiency with a low diastolic pressure, because coronary artery filling takes place during diastole, and a low diastolic pressure results in a low coronary blood flow.

B. Increased Oxygen Consumption.—This occurs in hyperthyroidism and severe anemias, for example.

C. A Combination of Decreased Coronary Blood Flow and Increased Oxygen Requirements.—This can produce myocardial anoxia even in the presence of a completely normal heart, as may occur for example during an attack of paroxysmal tachycardia (see page 343).

The Relation Between Angina Pectoris and Myocardial Anoxia.—Although angina pectoris is due to myocardial anoxia, it should be emphasized that myocardial anoxia can occur without anginal pain, even when the anoxemia is sufficient to produce necrosis of the heart muscle. This has been demonstrated for example, in cases of postoperative shock, acute hemorrhage, carbon monoxide poisoning, even in cases of massive myocardial infarction. Why some people develop severe pain and others none is obscure. The psychological make-up of the patient and his individual sensitivity to pain determine in large measure the severity, and even the duration of the pain. In this connection I should like to point out that many patients with angina pectoris are highly-keyed emotionally and intensely unhappy. Therefore, once an attack occurs, minor precordial aches and pains are often magnified by fear of death, or a desire for sympathy. This is one of the reasons that placebo therapy has proven effective in the treatment of angina pectoris.

Myocardial anoxia probably causes pain in a manner similar to that which occurs when a skeletal muscle, whose circulation has been impeded, is exercised. For example, it has been shown that if the arteries of an extremity are constricted and the extremity exercised until pain develops, release of the constriction is followed by a release of the pain in a few seconds, even though the exercise is continued. However, if the constriction is maintained but the exercise stopped when pain occurs, the pain continues until the circulation is restored.

The pain stimuli probably originate in the sensory fibers which run in the adventitia of the coronary arteries. From here, the stimuli are carried along sympathetic fibers by way of the middle and inferior cardiac nerves, or over the accessory cardiac rami, to the upper three thoracic ganglia. From here the impulses enter the spinal cord through the white rami communicantes and the posterior roots of the upper four thoracic segments.

Pathology.—During an attack of angina pectoris no pathological changes occur in the heart muscle because of the short duration of the anoxemia. However, if a patient dies during an attack, or develops "status anginosus" and dies after several hours, small scattered areas of myocardial necrosis may be present, scattered through the subendocardial region of the ventricles, even though the coronary arteries remain patent.

In patients who have had angina pectoris for some time, there can be usually found closure of one or more of the major coronary arteries at autopsy. Infarction of the heart need not be present if the closure of the vessel or vessels has been a slow process. Instead, there may occur death of only a small number of muscle fibers, resulting in subsequent fibrosis of the myocardium.

Symptoms.—The characteristic symptom of angina pectoris is pain. The pain has been variously described as oppressive, uncomfortable, vise-like, sometimes crushing, boring or burning, but not sticking. It may be associated with belching which gives relief, thereby deluding the patient into thinking that the attack is of gastrointestinal origin. The pain is characteristically substernal, but may be located over the left pectoral muscles near the apex of the heart. From the substernal and left pectoral regions it may radiate to the left shoulder and along the inner aspect of the arm to the elbow, the wrist and even to the ring and little fingers. Rarely it includes the thumb The pain may also radiate to the right shoulder and down the inner aspect of the right arm, but radiation to the right arm and not to the left arm practically never occurs.

Less common sites of radiation are to the jaw, the teeth or to the head and the interscapular region, or to the epigastrium. Occasionally, the pain begins in the jaw or arm, and spreads to the chest. Local hyperesthesia or tingling of the skin may occur, and patients may complain that the arm feels numb or "dead." The hyperesthesia may persist even after the anginal attack disappears With the pain, droplets of sweat may form on the patient's forehead and there may be intense salivation. There is no dyspnea but there may be a choking or smothering sensation in the throat. Often, there is a feeling of impending doom.

Precipitating Factors—The attack can be precipitated by such exertion as stair-climbing, walking in the cold or against the wind, or even slight exercise, especially after a full meal. In other cases, anger, fear, worry, excitement, sexual intercourse, straining at the stool, coughing and even sneezing may induce an attack. Occasionally the patient will be wakened from sleep, the attack having been brought on by a bad dream. Smoking and occasionally coffee-drinking can precipitate typical anginal seizures.

Frequency.—The frequency of attacks depends on the nature of the precipitating factors, and many patients who avoid emotional and physical stresses can keep reasonably free of attacks. Attacks may occur several times an hour, but some patients have only one or two attacks a year, and there are frequently long intervals of months or years of complete freedom from attacks.

Duration.—The attack strikes abruptly and the patient learns that by stopping what he has been doing, and standing or preferably sitting quietly, the pain will disappear in a few seconds or minutes. Rarely, the pain lasts fifteen minutes or more. Therefore, pain which persists more than one-half or one hour is not due to angina, until proved otherwise. After the attack, the patient frequently voids large quantities of light-colored urine.

Signs.—Examination of the patient during an anginal attack reveals surprisingly few abnormal signs The anxious appearance of the patient and the cold sweat that appears have already been noted Physical examination of the heart does not reveal any abnormal signs not previously present. The pulse and blood pressure may remain unchanged. Often, however, there is a rise in blood pressure during an attack. A fall in blood pressure during an attack of angina pectoris is suggestive of an impending myocardial infarct.

Fluoroscopic and X-Ray Examination.—No abnormal findings appear during the attack.

Electrocardiogram (Fig. 62).—The patient who suffers from angina pectoris may show a normal electrocardiogram, signs of old or healing myocardial infarction, or many other abnormalities, such as bundle branch block, ventricular hypertrophy or strain, abnormal *T* waves, *etc.*, none of which are specific for coronary artery disease During an attack, the electrocardiogram may remain unchanged. However, in many cases, characteristic changes in the *RS–T* segment occur, because of the myocardial anoxia,

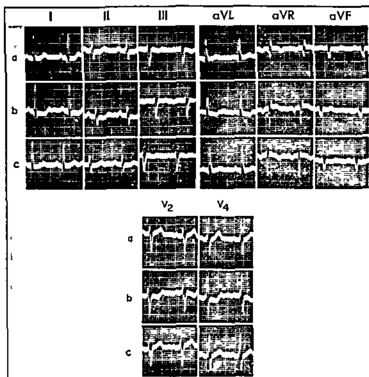


FIG 62—Myocardial anoxia (acute coronary insufficiency) induced by exercise *A*, Patient was sitting quietly *B*, Was taken immediately after exercise had produced an attack of angina pectoris *C*, Was taken three minutes later The anginal attack had spontaneously subsided. (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed, 1953)

or more specifically, because the anoxia affects particularly the subendocardial region of the ventricles. This causes depression of the *RS–T* segment in the standard leads, the precordial leads, and leads *aVL* and *aVF*, and elevation of the *RS–T* in lead *aVR*, for the following reason: When myocardial injury, due to anoxia, infarction, trauma, or any cause, is present, a unipolar lead that faces the surface of the injured muscle records an elevated *RS–T* segment, and a unipolar lead that faces the surface of uninjured muscle records a depressed *RS–T*. Because the injury affects the endocardial region of the heart, lead *aVR*, which faces the cavity of

Symptoms.—The characteristic symptom of angina pectoris is pain. The pain has been variously described as oppressive, uncomfortable, vise-like, sometimes crushing, boring or burning, but not sticking. It may be associated with belching which gives relief, thereby deluding the patient into thinking that the attack is of gastrointestinal origin. The pain is characteristically substernal, but may be located over the left pectoral muscles near the apex of the heart From the substernal and left pectoral regions it may radiate to the left shoulder and along the inner aspect of the arm to the elbow, the wrist and even to the ring and little fingers. Rarely it includes the thumb The pain may also radiate to the right shoulder and down the inner aspect of the right arm, but radiation to the right arm and not to the left arm practically never occurs

Less common sites of radiation are to the jaw, the teeth or to the head and the interscapular region, or to the epigastrium. Occasionally, the pain begins in the jaw or arm, and spreads to the chest. Local hyperesthesia or tingling of the skin may occur, and patients may complain that the arm feels numb or "dead" The hyperesthesia may persist even after the anginal attack disappears With the pain, droplets of sweat may form on the patient's forehead and there may be intense salivation. There is no dyspnea but there may be a choking or smothering sensation in the throat. Often, there is a feeling of impending doom.

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Fluoroscopic and X-Ray Examination.—No abnormal findings appear during the attack

A. The symptoms may suggest a noncardiac disorder. This is especially true if the discomfort begins in an unusual area such as the epigastrium, the arms or jaw, or if other symptoms, such as belching, apparent relief by bicarbonate of soda, or the occurrence of attacks following meals are a prominent part of the picture.

B. Other cardiac lesions may simulate angina pectoris. For example, substernal or precordial pain may appear in acute myocardial infarction (page 593), dissecting aneurism of the aorta (page 659), aneurism of the aorta (page 546), acute pericarditis (page 644), acute rheumatic carditis, neurocirculatory asthenia (page 310). In subendocardial myocardial infarction (page 598) the electrocardiogram may be identical with that of an ordinary anginal attack. Massive pulmonary embolism (page 619) may also produce intense substernal pain, due to reflex myocardial anoxemia. Severe anginal pain may also develop during an attack of paroxysmal tachycardia, especially if the patient suffers from coronary artery disease, and I have seen an attack of paroxysmal tachycardia precipitate status anginosus which was not relieved until the tachycardia was stopped.

C. Noncardiac disease may simulate the symptoms of angina pectoris Some of the more common noncardiac conditions that may cause substernal or precordial pain are the following:

1. **Lesions of the Cervical or Thoracic Vertebrae.**—Lesions, such as spondylitis, tumors, inflammatory lesions, even a ruptured intervertebral disc may cause diffuse pain, with local areas of tenderness over the spine, or the pain may be radicular in distribution, that is, confined to a band-like area of the anterior or posterior chest wall.

2 **Subdeltoid Bursitis, Periarthritis, or Fibrositis of the Left Shoulder.**—The pain may radiate along the points of attachment of the pectoral major muscle. It is usually aggravated by abduction and external rotation of the arm. Local points of tenderness can usually be found over the shoulder region, and *x*-ray examination may reveal calcification of the subdeltoid or subacromial bursa. Even though a patient with chest pain is found to have a left-sided shoulder lesion, this, itself, does not rule out angina pectoris, because the shoulder lesion may have developed as an aftermath of an attack of myocardial infarction (see page 603). Myositis of the left pectoral muscles can also cause precordial pain

3. **The Scalenus Anticus Syndrome** (page 140).

4 **Slipping Rib Cartilage Syndrome.**—This is usually due to trauma, and particularly affects the eighth, ninth, or tenth rib There is local tenderness of the rib on palpation. If the patient is placed on his back with the knees flexed, manipulation of the affected rib cartilage reproduces the pain, and an audible click can sometimes be heard. Treatment consists in strapping.

5. **Herpes Zoster of the Intercostal Nerves.**—Intense precordial pain may develop several days before the herpetic lesions appear and may last for months thereafter.

6 **Hiatus Hernia of the Stomach.**—In this condition, a portion of the stomach slips into the thorax through the esophageal opening of the diaphragm. Substernal pain or pressure may develop, radiating to the back and to the left shoulder and arm. The pain is worse on lying, tends to

the heart, shows a characteristic *RS–T* elevation (Figs. 53, *A*, page 205), whereas the other leads face varying portions of the epicardial surface of the heart and show depressed *RS–T* segments.

These changes disappear in a few minutes. Occasionally, the *RS–T* changes are delayed in appearance until ten minutes or more after the actual pain disappears Rarely, transient *RS–T* changes of the type that occurs in massive myocardial infarction appear, due to spasm of a large coronary artery

Ballistocardiogram.—Nonspecific abnormalities may be found in the ballistocardiogram in angina pectoris and in coronary artery disease in general (page 219) In some cases of angina pectoris with a normal resting electrocardiogram and ballistocardiogram, exercise may cause the ballistocardiogram to become abnormal, while the electrocardiogram remains normal This, however, is neither specific nor characteristic of angina pectoris

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In addition, there may be an elevated blood cholesterol level, abnormal phospholipid-cholesterol ratio, and abnormal serum lipoproteins of the S_f 10–20 class These abnormalities, however, are characteristic of atherosclerosis, rather than of angina pectoris (page 582).

Diagnosis.—Angina pectoris occurs particularly in middle age, especially in the fifties, but it is also common in the fourth decade, and even occurs at the age of thirty years or less. In young people, angina pectoris usually accompanies rheumatic or syphilitic aortic insufficiency, rheumatic aortic stenosis, rarely mitral stenosis, or hyperthyroidism or severe anemias. In such cases, the pain often occurs at rest and may last longer than half an hour.

In patients with angina due to aortic valvular disease, sinus tachycardia above 140, a marked increase in systolic blood pressure, even above 250 mm., and marked throbbing of the head often accompany the attacks. These patients obtain excellent relief from the nitrites, especially amyl nitrite, and even by walking during an attack.

Angina pectoris due to coronary artery disease is also becoming more frequent in the younger age groups. Men are affected more than women, white people more than negroes There is also a high incidence of diabetes in patients who have angina. The diabetes is probably one of the factors contributing to the coronary artery disease.

When a middle-aged patient complains of attacks of substernal and left pectoral oppression, which may spread to the head, the inner aspect of the arms, and even the epigastrium, precipitated by exertion, emotional tension, or cold, and lasting from a minute or so to about fifteen minutes, a diagnosis of angina pectoris can justifiably be made, especially if the attacks are relieved by nitroglycerin or momentary rest. However, when all these features are not present, the diagnosis can be very difficult to make. Difficulties in diagnosis are usually due to one of the following factors:

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The Use of Tests Which Induce Myocardial Anoxia in the Diagnosis of Angina Pectoris.—The diagnosis of angina pectoris in the past has depended more or less on the validity of the patient's story and symptoms, because the findings on physical examination are often normal Since the electrocardiogram during an attack often shows changes due to myocardial anoxia, many attempts have been made to reproduce the anginal attack under standardized conditions by means of exercise, or by induced anoxemia, using the electrocardiographic patterns which appear as a means of diagnosis

The great difficulty with this method is that angina pectoris is a symptom, whereas the electrocardiographic patterns which appear are due to myocardial anoxia; and while it is true that angina pectoris occurs as a manifestation of myocardial anoxia, attacks of angina may occur without the development of abnormal electrocardiographic patterns, and myocardial anoxia may occur with characteristic electrocardiographic patterns but without the appearance of anginal pain

This can occur not only during an exercise or anoxemia test, but as a result of conditions such as shock, acute hemorrhage, carbon monoxide poisoning, massive pulmonary embolism, *etc*, all of which can precipitate myocardial anoxia.

1 *Exercise Tests.*—Various forms of exercise can be used. The patient may be asked to hop or do knee-bending exercises, or actually climb stairs, or step over a two-step staircase until pain or dyspnea occurs Graded exercises can also be used. It has been found that optimum exercise for precipitating the anginal attack is 20 trips over a two-step staircase (corresponding to climbing two flights of stairs) done under the following standardized conditions. low room temperature, between 45 to 50° F , one hour after a light breakfast; no recent attack—the patient rests for fifteen minutes before the exercise, and if there has been a recent anginal attack, the rest period is an hour, no medication for twelve hours, familiarity of the patient with the test.

To conclude, exercise tests have limited value in the diagnosis of angina pectoris because a positive result merely indicates that myocardial anoxemia has been induced and not that angina pectoris is present The reason for this is that myocardial anoxemia may occur in the absence of angina pectoris. However, when exercise reproduces anginal pain, and positive electrocardiographic changes appear, the diagnosis of angina pectoris can be accepted. On the other hand, a negative exercise test does not rule out angina pectoris. It should also be pointed out that while exercise tests are comparatively safe, I know of two patients who died immediately following the exercise (Fatalities can be prevented by following the rules given above and limiting the exercise to 20 trips over a two-step staircase)

Regardless of the type of exercise, one of the following reactions will occur.

a Anginal-like pain develops and the electrocardiogram shows marked RS–T changes typical of myocardial anoxia The diagnosis in such a case is obvious However, if the *RS–T* deviations are not marked, the result may be difficult to interpret, especially since there is disagreement as to what constitutes an abnormal electrocardiographic response to exercise.

disappear on standing It is noted especially after meals, and at night, after retiring The pain is precipitated by any condition that increases intraabdominal pressure, such as bending, coughing, straining at the stool, physical exertion There is also some degree of dysphagia present, with acid regurgitation and vomiting The stools may show occult blood. X-ray examination of the upper gastrointestinal tract shows part of the stomach above the diaphragm

7. **Esophageal Diverticula** —There is a complaint of food sticking in the chest, and of regurgitation of food which has the same taste as that swallowed There is no acid regurgitation X-ray examination shows the diverticulum, or multiple diverticula

8 **Cardiospasm** —Spasm of the esophagus at the point of its passage through the diaphragm may cause intense substernal pain or pressure. In the early stages the pain is intermittent and associated with a feeling of food stopping and sticking near the level of the xiphoid process Later the pain may become constant and may last for several days at a time. The pain is not related to exercise X-ray examination of the esophagus reveals it to be dilated but tapering sharply where it penetrates the diaphragm

9 **Ulcers of the Esophagus, Stomach or Duodenum.**—Such lesions may cause epigastric and low substernal pain. Chronic gall bladder disease may also produce pain similarly located

10 **Mediastinal Emphysema** (page 600).

11 **Diaphragmatic Flutter.**—In this condition, spasmodic, rapid contractions of the diaphragm occur On auscultation, the sounds produced by the contracting diaphragm may simulate the irregular heart action of auricular fibrillation However, the pulse and the electrocardiogram reveal that the heart is beating normally.

12 **Pulmonary Hypertension** —Anginal-like pain can occur in conditions associated with pulmonary hypertension, such as mitral stenosis, chronic pulmonary disease, especially emphysema, bronchiectasis, bronchial asthma and generalized pulmonary fibrosis, and congenital heart lesions with pulmonary hypertension, such as the Eisenmenger complex, auricular septal defects and patent ductus arteriosus

Such patients usually show the following:

a A history of long-standing cough.

b. Cyanosis, which is intermittent or persistent. (This is the reason that angina occurring in these patients had been called *angina hypercyanotica.*)

c Association of dyspnea with the pain.

d Variability of the duration of the pain, which may persist for days, weeks or months, with or without aggravation on exercise.

e. Clinical signs of right ventricular hypertrophy.

Such patients obtain marked relief from inhalation of oxygen. Aminophylline is also helpful Nitrites are not effective.

D The patient may have angina pectoris in addition to noncardiac disease. In such cases, a diagnosis may be very difficult.

E. In many instances, language difficulties, emotional instability, inadequate observation or vagueness of the symptoms may make it impossible for the patient to present a clear picture of his sensations

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For example, it has been stated that significant electrocardiographic changes consist of *RS–T* depression of more than 1.5 mm. in the standard leads, and 2 mm in precordial lead *IVR* (chest electrode just outside the apex of the heart—the other electrode on right arm), or a change in the sign of the *T* wave, except if it occurs in lead III alone. Another criterion, based on a graded two-step test, consists of a depression of the *RS–T* segment of more than 0.5 mm in any lead, or a change from an upright *T* to an isoelectric *T*, or change in the direction of the *T* wave.

I believe that the only significant changes are an elevation of the *RS–T* in lead *aVR* of 1 mm or more, associated with *RS–T* depression in any of the unipolar precordial leads or in lead *aVL* or *aVF* of 1 mm. or more, because I have observed on many occasions marked *T* wave changes after exercise in young, normal people. Furthermore, if the control tracing shows bundle branch block or left ventricular strain, even *RS–T* deviations may be difficult to interpret. If the control tracing shows signs of myocardial infarction, even old, the exercise test should not be used.

If the patient is taking a digitalis preparation, marked *RS–T* deviations may occur after exercise, even if angina pectoris is not present.

The changes which occur should disappear in a few minutes. If the changes persist, the possibility of subendocardial infarction (page 598) must be considered.

b. Anginal-like pain develops but the electrocardiogram remains essentially unchanged. In such a case, the exercise test has no significance, and the diagnosis of angina must rest on the patient's history.

c. No anginal pain occurs but the electrocardiogram shows abnormal RS–T deviations. In such a case, a diagnosis of myocardial anoxemia can be made. This is presumptive but not pathognomonic evidence that the patient's pain is anginal in nature. However, the pain may be due to a noncardiac condition. In addition, abnormal *RS–T* deviations may appear in many elderly people who have no complaints.

d. No anginal pain occurs and the electrocardiogram remains unchanged. Such a negative test does not rule out the diagnosis of angina, because the patient's capacity for exercise can vary markedly even during the course of the day, and a patient, who in the morning will develop anginal pain by climbing one flight of stairs, may be able to climb nine or more flights of stairs in the afternoon without developing pain. Another factor to be considered when the electrocardiogram remains unchanged is that changes sometimes do not appear until ten or more minutes after the exercise.

2. *Anoxemia Tests.*—Inasmuch as exercise may not produce characteristic electrocardiographic signs in patients with angina pectoris, many investigators have attempted to reproduce myocardial anoxia, at rest, by having the patient breathe a mixture sufficiently low in oxygen to precipitate myocardial anoxia in patients with coronary artery disease, but not low enough to cause anoxia in normal people. This can be best accomplished by having the patient breathe a mixture of 10 per cent oxygen and 90 per cent nitrogen for twenty minutes. However, here again, a positive result indicates the presence of myocardial anoxia, and not necessarily angina pectoris, because patients who never had an anginal attack may develop abnormal *RS–T* deviations. Conversely, patients may develop

anginal symptoms within a few minutes after the test begins, even though the electrocardiogram remains unchanged. Like the exercise test, the anoxia test may prove dangerous, and acute pulmonary edema, acute myocardial infarction, convulsive seizures and even death have followed the test

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If the patient is taking a digitalis preparation, marked *RS–T* deviations may occur after exercise, even if angina pectoris is not present

The changes which occur should disappear in a few minutes. If the changes persist, the possibility of subendocardial infarction (page 598) must be considered

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d No anginal pain occurs and the electrocardiogram remains unchanged. Such a negative test does not rule out the diagnosis of angina, because the patient's capacity for exercise can vary markedly even during the course of the day, and a patient, who in the morning will develop anginal pain by climbing one flight of stairs, may be able to climb nine or more flights of stairs in the afternoon without developing pain. Another factor to be considered when the electrocardiogram remains unchanged is that changes sometimes do not appear until ten or more minutes after the exercise.

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myocardial infarct, with oxygen and anticoagulant therapy (page 605), and kept in bed for about a week.

Drug Therapy —Innumerable drugs have been used to prevent attacks of angina pectoris In fact, placebos are frequently of value. The following are some of the drugs which have been found effective: nitrates, xanthines, papaverine and its synthetic analogue, paveril (dioxyline phosphate), testosterone, deproteinated tissue extracts, such as depropanex, alcohol, sedatives, khellin, anticoagulants such as heparin. A few of these will be considered in more detail.

The Nitrites —The term nitrite includes inorganic nitrites and nitrates such as sodium nitrite and bismuth subnitrate, and organic compounds such as amyl nitrite, glyceryl trinitrate (nitroglycerin), erythrol tetranitrate, mannitol hexanitrate or pentanitrate, and octyl nitrite, which act by liberating the nitrite ion which relaxes smooth muscle, such as the coronary arteries and the finer blood vessels, especially venules and capillaries The result is coronary artery dilatation, marked peripheral vasodilatation, and a drop in blood pressure Because of the vasodilatation and the fall in blood pressure, compensatory tachycardia may occur. This is especially seen after amyl nitrite. In addition, dizziness, a sense of heat and blushing of the face and neck, and throbbing of the head and pulse may occur, even headache Nausea, vomiting and syncope can also appear if marked pooling of blood occurs in the lower extremities With continued use of massive doses of the nitrites, cyanosis due to methemoglobinemia may occur.

In some cases, the nitrites may aggravate the angina and may produce or aggravate the electrocardiographic pattern of myocardial anoxia.

The presence of glaucoma is a contraindication to the use of the nitrites

Nitroglycerin is usually prescribed in tablets of 0 03 to 0 06 mg. ($\frac{1}{200}$ to $\frac{1}{100}$ grain) strength, to be placed under the tongue and dissolved in the mouth The small hypodermic tablets are better than the larger triturated tablets because they dissolve faster. When the tablets become hard after a few months exposure to the air, they lose their potency. Therapeutic effects occur in one to two minutes and last thirty minutes. Occasionally, side reactions are so strong that the dose must be decreased to 0 015 mg. ($\frac{1}{400}$ grain). The smallest effective dose should be used.

Amyl nitrite is supplied in fragile glass ampoules, called pearls, containing 3 or 5 minims, which are crushed in a handkerchief and inhaled An effect occurs within half a minute and lasts less than ten minutes

Other Nitrites —The other preparations do not begin to take effect for five to fifteen minutes and are therefore best suited for prophylactic use. The dose of sodium nitrite is 15 to 60 mg ($\frac{1}{4}$ to 1 grain), 3 times a day. The dose of erythrol tetranitrate is 30 to 60 mg. ($\frac{1}{2}$ to 1 grain), 3 times a day. The dose of mannitol hexanitrate is 15 to 30 mg. ($\frac{1}{4}$ to $\frac{1}{2}$ grain) 3 times daily. Nitroglycerin, $\frac{1}{200}$ to $\frac{1}{100}$ grain may also be taken prophylactically a few minutes before performing strenuous work, or doing anything that may precipitate an attack.

Peritrate is one of the newer nitrites in clinical use. It is a nitric acid ester of the tetrahydric alcohol, pentaerythritol. It is similar to nitroglycerin in its action, but has a slower absorption (one and a half hours) and a more prolonged action (four to five hours)

Peritrate cannot be used for an acute attack because of its slow absorption, but can be used to prevent attacks of angina pectoris The average oral dose is 1 tablet (10 mg.) four times daily. Some patients require as much as 2 tablets three or four times a day for maximal relief

Side reactions occur even with small doses of peritrate as with all the nitrites.

Tolerance develops to the nitrites in about two to three weeks, after which even massive doses give little relief, and I have seen patients consume 50 or more tablets of nitroglycerin daily with but little relief of the anginal symptoms When tolerance develops, the nitrites should be discontinued for a week or two, after which, small doses are again effective

The Xanthines.—Theobromine and theophylline and their salts (page 215) have been used extensively in the prophylaxis of angina pectoris They have been found highly effective by some cardiologists and of only placebo value by others I have used them, but am not convinced of their efficacy when given orally. However, 0 5 gram aminophylline given intravenously, intramuscularly or in the form of rectal suppositories has proven helpful

Recently, oral preparations of aminophylline, containing aluminum hydroxide, which do not irritate the gastrointestinal tract as much as ordinary aminophylline, have been available Therefore, as much as 1 gram or more of aminophylline can be given daily.

Two of these preparations are Aminodrox tablets (1½ and 3 grain strength), and Cardalin tablets (each containing 5 grains of aminophylline with aluminum hydroxide and ethyl aminobenzoate)

Papaverine —Papaverine in doses of 0 1 gram (1½ grains) 4 or 5 times daily has also been recommended because of its vasodilating action Results have not been spectacular When larger doses are used, the drug often acts as a hypnotic, and may cause annoying sweating.

Testosterone Propionate —The male sex hormone has been effective in my experience. Whether it acts as a vasodilator or merely by promoting a sense of well-being is not known It is usually given intramuscularly in doses of 25 mg , every second to fifth day for a total of 5 to 25 injections, the average being 12

Alcohol.—Alcohol (whiskey, brandy, rum) has been used for many years in the treatment of angina pectoris I have prescribed it in moderate quantity—an ounce several times a day—and while I have not made alcoholics of any of my patients, I also have not cured any of them with it. It does however relieve mental tension, and in this way diminishes the number of attacks Preparations, such as crème de menthe, are of value in relieving "gas" of which so many patients complain.

Sedatives —Sedatives are helpful in relieving mental tension The barbiturates can be used, but I have found bromural, 0 3 gram (5 grains) 3 times daily, or chloral hydrate, 0 3 gram (5 grains) several times a day very effective. The following prescription can be written for the chloral hydrate·

℞ Chloral hydrate	5
Syr auranti	60
S teaspoon after meals	

Often even smaller doses are effective. When chloral hydrate is prescribed, alcohol should be forbidden, because of its potentiating effect on chloral

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Anticoagulant Therapy.—Two types of anticoagulant therapy have been used in angina pectoris:

A. In patients with long-standing angina pectoris, heparin has been given intravenously in a dose of 100 mg, twice a week for several months. Recent observations, however, indicate that heparin is no more effective than the placebo injection of saline

B Anticoagulant therapy with either heparin, dicumarol, *etc.*, has been used in patients whose anginal attacks are becoming more severe, in an attempt to prevent coronary artery occlusion and myocardial infarction In many of these patients, the infarct develops in spite of the anticoagulant therapy (There is a theoretical possibility that anticoagulant therapy given at this time—before coronary occlusion occurs—may help precipitate the occlusion by causing subintimal hemorrhage of a coronary artery—see page 593)

Surgical Procedures.—Attempts have been made to interrupt the path of the painful stimuli to the central nervous system by means of section of the upper four or five dorsal roots (posterior rhizotomy), or thoracic sympathectomy, or preferably, by paravertebral nerve block of the upper four thoracic nerve roots, using alcohol Nerve block may be very effective, but pleuritis may develop if the pleural space is penetrated, and marked hyperesthesia of the skin of the chest wall or arm occasionally develops This may be more annoying than the original anginal attacks. After the nerve block is done, the patient must be warned against excessive work, because the nerve block does not increase coronary blood flow, and the warning signal of pain is no longer present.

Attempts have been also made to increase the coronary circulation surgically by pericardial transplants of subpectoral muscle or omentum, and even by dusting talc into the pericardial sac to produce pericardial adhesions The great cardiac vein has also been ligated and other operations done in an attempt to improve the coronary circulation. Such procedures must still be considered experimental.

Local Anesthesia.—A simple procedure is to palpate carefully the thorax for sensitive points in or beneath the skin, the so-called "trigger points," and to infiltrate these areas with 1 per cent procaine solution, or to spray the region with ethyl chloride. This may cause the anginal pain to diminish or even to disappear.

Total Thyroidectomy—This has also been used in the treatment of angina. The rationale of this is that with the decreased metabolic needs of the body, the coronary circulation becomes more efficient. More recently, the oral administration of propylthiouracil and other antithyroid compounds, and radioactive iodine have been used, with some success.

Airplane Travel.—Travel by air may prove hazardous for the patient with angina pectoris or coronary artery disease (or congestive heart failure), because flying at an altitude of 10,000 feet is equivalent to breathing a gas mixture containing only 14 per cent oxygen, and although most commercial airliners fly at an altitude of 8,000 feet or less, it is sometimes necessary to bring the plane up to 20,000 feet.

There are two methods by which the tendency to anoxemia can be overcome: first, the continuous use of oxygen breathing equipment during the

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Signs.—On physical examination, a worried expression and dilated pupils may be noted. The skin is likely to show flushing, especially of the face and neck. The hands are cold and clammy, and mottled with a red or cyanotic hue, and there may be a coarse tremor of the outstretched fingers A low-grade fever may develop, the rectal temperature rising as high as 102°F A characteristic sighing type of respiration, described above, is often noted The patellar and Achilles deep tendon reflexes are brisk and hyperactive.

Examination of the heart usually reveals a sinus tachycardia. Rarely, palpitation may be due to an attack of paroxysmal tachycardia or paroxysmal auricular fibrillation of flutter Systolic, apical or pulmonary murmurs may be present, and there may be accentuation of the heart sounds due to the sinus tachycardia, with a snapping first sound

Fluoroscopic and X-Ray Examination.—On fluoroscopy, the heart is found to be normal in size, but pulsations may be exaggerated.

Electrocardiogram.—The tracing is normal. Occasionally, flat or downward *T* waves appear in leads II, III, *aVF*, and even in the precordial leads, similar to changes that may occur normally on standing.

Laboratory Tests.—Circulation time tests, venous pressure, basal metabolic rate, sedimentation rate and red and white blood counts are normal. There is some disturbance in the functional ability of the patient to undertake work, because on exertion, the blood lactic acid level rises abnormally high. The vital capacity, and breath-holding ability (see below) may be low because of inefficient use of the respiratory muscles.

Diagnosis.—Not every patient experiences all the symptoms described above. In some, the cardiorespiratory symptoms, in others gastrointestinal or neuromuscular complaints predominate. If cardiorespiratory complaints are present, and in addition, if the patient complains of arthralgia and runs a slight fever, and if a systolic murmur is heard, along with a tachycardia and a sharp first apical sound, neurocirculatory asthenia simulates acute rheumatic fever However, the normal white count and sedimentation rate, the lack of relation between the multiplicity of symptoms and the paucity of clinical findings, the presence of marked sweating, tremor, facial flush, and cardiorespiratory symptoms allow the diagnosis of neurocirculatory asthenia to be made. However, one should remember that neurocirculatory asthenia may occur in a patient with organic heart disease. In such a case, the condition is often called a cardiac neurosis, and the differentiation of symptoms due to the asthenia and those due to the organic lesion is very difficult.

Neurocirculatory asthenia can also simulate hyperthyroidism, but the basal metabolic rate is normal, the hands are cold, not warm, there is no exophthalmos, and the tremor of the hands is coarse and not fine. Occasionally, tuberculosis or other chronic infections, such as brucellosis, are erroneously diagnosed.

Various tests have been used in diagnosis, the most simple of which is the breath-holding test. Here, one measures the time the breath can be held after a full inspiration. Normally this should exceed half a minute However, breath-holding ability of less than this may be due to chronic pulmonary disease, incipient heart failure, generalized debility, as well as

Chapter 17

NEUROCIRCULATORY ASTHENIA

THE syndrome of neurocirculatory asthenia (daCosta's syndrome, effort syndrome, disordered action of the heart, irritable heart, functional cardiovascular disease, *etc.*) differs from the syndromes previously described in this Section, in that neurocirculatory asthenia is not associated with cardiovascular pathology. Nonetheless, it is important to recognize the protean manifestations of neurocirculatory asthenia because early and prompt therapy may effect a cure, and because it can mimic more serious disorders, such as acute rheumatic fever, thyrotoxicosis, and even heart failure.

Etiology.—Neurocirculatory asthenia occurs most commonly among young adults, but it may occur at any age It is related to mental or psychic stress and occurs particularly in people who are unable to make adequate emotional adjustments to the rigors of life In some cases, it may occur as an acute episode in otherwise well-balanced persons who have been suddenly subjected to intense and unusual stress, physical or mental. Therapy is comparatively easy in such cases. In others, the condition is present in chronic form Psychiatric analysis of such cases has led to diverse results but many of the patients have a narrowed range of emotional and physical activity, and a disinterestedness and unconcern with many aspects of their environment. These patients are emotionally immature, oversensitive, and have a morbid preoccupation with their bodily functions; and it would seem that the physiological disturbances which occur act as a prop and a psychological excuse for the inability of the patient to carry on even the ordinary physical activities of life

Symptoms.—The patient's complaints are multitudinous and may include fatigue, mental as well as physical, precordial pain, palpitation, tachycardia, dyspnea, giddiness, anorexia, nausea and vomiting, even diarrhea In addition, headaches and arthralgic and myalgic pains may occur. Palmar and axillary perspiration may be profuse.

A characteristic feature of the cardiorespiratory symptoms is that they occur at rest as well as on exercise, and are precipitated by emotional tension. The pain is usually a dull precordial soreness, most marked around the left nipple, lasting hours. However, with palpitation, a sharp, transient, sticking precordial pain may appear Long-lasting tenderness of the left pectoral muscles is common.

The dyspnea is often of the sighing type—the patient takes a deep breath and slowly exhales with a sigh of resignation. However, respiration is often shallow and irregular and involves excess use of the intercostal muscles rather than the diaphragm. With hyperventilation, giddiness may occur, though syncope is rare.

Signs.—On physical examination, a worried expression and dilated pupils may be noted. The skin is likely to show flushing, especially of the face and neck. The hands are cold and clammy, and mottled with a red or cyanotic hue, and there may be a coarse tremor of the outstretched fingers A low-grade fever may develop, the rectal temperature rising as high as 102°F. A characteristic sighing type of respiration, described above, is often noted. The patellar and Achilles deep tendon reflexes are brisk and hyperactive.

Examination of the heart usually reveals a sinus tachycardia Rarely, palpitation may be due to an attack of paroxysmal tachycardia or paroxysmal auricular fibrillation of flutter. Systolic, apical or pulmonary murmurs may be present, and there may be accentuation of the heart sounds due to the sinus tachycardia, with a snapping first sound

Fluoroscopic and X-Ray Examination.—On fluoroscopy, the heart is found to be normal in size, but pulsations may be exaggerated.

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neurocirculatory asthenia. For this reason, the following modification of the breath-holding test, the hyperventilation test, has been recently devised: The hyperventilation test consists in having the patient hold his breath (by holding his nose with his fingers) after a preliminary deep inspiration, as long as he is able to (the patient is allowed to exhale during this period). The number of seconds he refrains from inhaling is noted. Then, he is allowed to breathe normally for three minutes. The pulse rate is then determined, and he is instructed to breathe deeply and rapidly for forty-five seconds during which he takes 45 deep inspirations. Immediately at the end of this period of hyperventilation, the pulse is determined and he is instructed again to hold his breath The number of seconds he refrains from breathing is again noted.

In normal persons and even in patients with intrinsic cardiac or pulmonary disease, the breath-holding capacity after hyperventilation is usually much greater (often 30 per cent or more) than before. In patients with neurocirculatory asthenia, the breath-holding capacity remains about the same or diminishes after hyperventilation.

The pulse rate in normal subjects either remains constant or rises less than 20 per cent. In patients with neurocirculatory asthenia, marked acceleration of the pulse occurs with the above test.

Prognosis.—The patient who first manifests signs of neurocirculatory asthenia during a period of intense stress has an excellent chance of recovery. The prognosis for those who show signs of the condition in chronic form is less bright Such patients frequently drift from one doctor to another, seeking preferably those physicians who diagnose their complaints as signs of organic disturbances, and shying from the astute physician who makes the correct diagnosis of a functional condition.

Treatment.—The treatment of choice is psychotherapy. However, this is usually difficult because most of the patients with neurocirculatory asthenia are unwilling to accept psychotherapy as such By psychotherapy is meant an attempt to make the patient understand the meaning of his symptoms and the nature of his conflicts. It is really a process of emotional reeducation, and does not merely consist in giving the patient reassurance or in sending him off on a vacation On the other hand, it is not psychoanalysis, although many of the technics developed by the analysts can be used to advantage. It consists in a series of interviews in which the patient is encouraged to talk about those aspects of his life which have resulted in conflict or repression in the past. In other words, the patient is reexposed, under favorable conditions, to emotional situations which he was not able to handle in the past.

In carrying out treatment, certain principles should be constantly kept in mind:

1. The patient's confidence must be gained at the first office visit. There are many ways of doing this, and each successful physician has a method of his own. The attitude of the physician should be friendly rather than coldly professional, and the patient should feel that the doctor is taking a personal interest in his case. It is often advisable to spend the first few minutes in general conversation, talking about the patient's hobbies, things he likes to do, *etc*.

2. The emotional background of the patient, or in other words, the patient behind the disease, must be understood. This can be obtained in a general way even in the first visit by a careful history, in which relations between the onset of symptoms and the appearance of difficult life situations are noted For example, statistical data is important only insofar as it affects the patient. Thus, a notation that the patient's father died at the age of sixty-two years is meaningless, because the patient may not have seen his father for twenty or more years. Much more important is to ask, "Were you with your father when he died, or during his sickness? How did you react to his death? Did you have a breakdown and have to stop work?" The answers to these and other questions provide a good guide to the emotional and physical make-up of the patient and his ability to withstand stresses

No absolute rules can be laid down, and each patient must be treated individually However, the following are some of the points that can be elicited, and some of the questions that can be asked Actually, no set list of questions should be used, because much more pertinent and valuable information is often obtained by indirect questioning, rather than by a direct question-and-answer type of interview. Similarly, much important information can often be obtained from relatives rather than from the patient himself.

I frequently begin by telling the patient, "I am going to ask many questions Some of these will not appear to have any relation to your illness However, all of them are necessary and you should really try to answer them."

A. Present Illness "Since when are you sick? Were you completely well before this date? Do you remember exactly when you first felt this way? Where were you? What were you doing? Had anything unusual happened that day or around that time? What did you do when you first felt ill? Treatments? What happened since then? Now what bothers you mostly? Anything else? To what do you think your sickness is due? How do you think it can be cured? What would you do if it were cured?"

B Family Relation "Is your father living? With whom does he live? Is he ill? What type of person is he? Is he a heavy drinker?" Or, "When did he die? How old were you then? Where you with him at the time? How did you react to his death? Did you have to stop work? Is your mother living? *etc* Have you any brothers or sisters? *etc* Are there any nervous disorders or sicknesses in the family? *etc*

C Childhood "Did you always live with your parents when you were single? Were you often punished as a child? Were you happy at home?"

D Education "What subjects did you like?—dislike? When did you leave school? Why? Are you sorry?"

E Work: "What was your first job? Did you like it? Why did you choose it? How long did you keep it? Why did you leave? Other jobs?"

F Accidents and Illnesses.

G. Sexual Life "How old were you when you began to masturbate? Who taught you? How did you feel about it? How often do you still do it? How old were you when you first had sexual relations? How did you feel about it? Is your sex life now satisfactory? Why not? Did you ever have

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In questioning a woman. "When did you begin to menstruate? Were you prepared for it? How do you like it?"

II. General Questions. "Did you ever see anyone die? Did you ever see anyone suffer great pain? How do you react in a situation you can't control? Thunder? Water? Swimming? People?"

3 Following the history a careful physical examination and cardiovascular survey is done. At the conclusion of this, the patient is informed that he is suffering from an illness as real as if he had cut his finger or developed pneumonia, but that it is due to the fact that his organs are just not working right, even though each is healthy, and that you, the doctor, are confident that his symptoms can be alleviated and possibly (or probably) made to disappear (depending on the chronicity of the disorder).

4 In giving psychotherapy, the physician must remember that the patient will respond to him in an emotional way. Freud called this emotional reaction of the patient to physician, transference. In transference, the patient transfers to the physician his emotional behavior patterns based on the patient's past experiences, and the patient entertains toward the physician the same feelings and conflicts he has had in the past toward some person of authority (father, mother, step-parent, sibling, *etc.*). However, in the course of the interviews, the patient learns that he can actually express antagonism toward the physician without being punished, and can assert himself without being censured, and he gradually gains an emotional perception that he is no longer a child (emotionally) and is capable of living in an adult world emotionally as well as physically.

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5 Other Therapy.—Even without actual psychotherapy, patients often show improvement. Mild sedatives are often helpful, and it may be necessary at first to use placebo therapy and injections, although the psychiatrists frown on this. Injections of thiamine or testosterone are sometimes helpful in giving the patient a sense of well-being. Whether they have pharmacological or placebo value is difficult to determine. Smoking should be curbed as well as excessive use of coffee, tea, "cola" drinks, and alcohol.

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Chapter 18

THE CARDIAC ARRHYTHMIAS SINUS RHYTHMS, NODAL RHYTHM, *A-V* BLOCK, *A-V* DISSOCIATION

Introduction – The heart begins to beat automatically and rhythmically during early embryonic life and continues to beat until death occurs. These beats arise in the neuromuscular tissues of the heart, consisting of the sinus node, the *a–v* node, the bundle of His and its right and left branches, and the Purkinje fibers. Under certain conditions, stimuli may also arise in the auricular or ventricular muscle.

The sinus node (*s–a* node, sinoauricular node, or node of Keith and Flack) is a small, comma-shaped mass of tissue which resembles both muscle and nervous tissue. It is about 25 mm long and 2 to 5 mm. wide, and lies in a groove (the sulcus terminalis) between the opening of the superior vena cava and the right auricular appendage.

The *a–v* node (auriculoventricular node, or node of Tawara) is a specialized neuromuscular bridge between the auricles and ventricles. It is about 5 mm long and 2 to 3 mm wide. It lies in both the interauricular and interventricular septa, below and to the right of the opening of the coronary sinus. Anatomically, an upper, middle and a lower portion of the *a–v* node have been described.

The bundle of His is a direct continuation of the *a–v* node. It is about 10 mm long and 3 mm. wide. It runs along the top of the interventricular septum and then divides into a right bundle and a left bundle. The right bundle lies under the endocardium of the interventricular septum. It runs along the septum and when it reaches the endocardium of the right ventricle, it divides into smaller branches and finally ends in a fine network of Purkinje fibers, which penetrate the right ventricular muscle.

The left bundle crosses over to the left side of the interventricular septum and near its beginning, gives off a small branch which stimulates the upper left side of the septum. Beneath the endocardium of the left ventricle, it divides into small branches and terminates in the Purkinje network which penetrates the left ventricle.

There are also additional neuromuscular connections between the auricles and ventricles (accessory bundles of Kent). In certain cases, a stimulus may pass from the auricles to the ventricles by way of these connections in addition to passing through the *a–v* node (Wolff-Parkinson-White syndrome, page 375)

Classification of Cardiac Arrhythmias.—Normally, the sinus node forms stimuli at a faster rate than the other neuromuscular tissues of the heart. Thus the sinus node is the primary pacemaker of the heart, and controls the rate at which the heart normally beats. When stimulus formation in

the sinus node is depressed or ceases, secondary pacemakers, such as the *a–v* node, the bundle of His and its branches and even the ventricular muscle, can form stimuli and keep the heart beating. Stimulus formation in the *a–v* node is usually slower than in the sinus node. It is still slower in the branches of the bundle of His and slowest in the Purkinje fibers and the ventricular muscle However, under certain abnormal conditions, stimuli can be formed in any of these secondary pacemakers at a very rapid rate

Although stimulus formation is automatic, it can be modified by way of sympathetic and vagal fibers acting on the sinus and *a–v* nodes. The sympathetic system has a stimulating action on the heart, and the parasympathetic or vagal system has a depressing effect. However, the vagus and sympathetic nerves influence different portions of the heart unequally. The sinus node and the *a–v* node are predominantly under vagal influence, and an increase in heart rate is due to a decrease in vagal tone rather than to increased sympathetic activity. There is some evidence that the right vagus nerve controls the sinus node, and the left vagus nerve, the *a–v* node The ventricles, however, are under sympathetic control only

In the normal heart, the stimulus begins in the sinus node It then spreads through the auricular muscle and reaches the *a–v* node Here it is delayed for a time Then the stimulus spreads from the *a–v* node through the bundle of His, its branches, the Purkinje fibers, and then through the ventricular muscle. This normal sequence of the stimulation of the auricles and ventricles is known as sinus rhythm or regular sinus rhythm. It is the basic normal rhythm of the heart.

Arrhythmias or changes in the rhythm of the heart can occur in many ways Stimuli may arise in the sinus node more rapidly or more slowly than normal, or may cease. The auricles and ventricles can respond to stimuli that arise in the *a–v* node or other secondary pacemakers in the auricles or ventricles Finally, stimuli that arise in the auricles may be unable to spread through the *a–v* node for many reasons, and the auricles and ventricles then beat independently of each other

The more common cardiac rhythms can be classified in the following way

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Symptoms.—Symptoms such as palpitation may occur when the heart rate suddenly increases with exercise. If the heart rate suddenly slows, dizziness or even syncope may result.

Signs.—A slow full pulse is present. The rhythm is usually quite regular. The neck veins show a systolic collapse, indicating that the bradycardia is of sinus origin (see page 150).

Electrocardiogram.—Sinus rhythm is present at a rate below 60 The *P–R* and *Q–T* intervals tend to become longer as the heart slows (Fig 63).

Diagnosis—A slow regular heart rate below 60 can occur not only in sinus bradycardia, but in nodal rhythm (page 322), incomplete *a–v* block of the 2·1, 3:1, *etc.*, type (page 326), complete *a–v* block (page 327), or auricular fibrillation or flutter with a slow ventricular rate (usually due to excessive digitalis) (page 367). Differentiation of these conditions can often be made by observing the neck vein pulsations while the radial pulse is being palpated (page 150).

Course and Prognosis.—Sinus bradycardia itself has no clinical significance.

Treatment.—No treatment is indicated.

Sinus Tachycardia.—Sinus tachycardia is arbitrarily described as a sinus rhythm faster than 100 beats per minute. The rate may become as rapid as 180 or more a minute. Usually the rate is less than 140.

Etiology.—Sinus tachycardia is due to a release of vagal tone, or to sympathetic stimulation of the sinus node, or to a combination of both factors Infants and children normally show a sinus tachycardia The rate at birth averages 110 to 150, at two years, 85 to 125, at four years, 75 to 115, at six years, 65 to 105 After six years, the heart rate of a resting child is usually less than 100

Sinus tachycardia may also occur in normal adults, even at rest. It occurs on exertion and excitement. Drugs, such as atropine, epinephrine, amyl nitrite, even tea and coffee, alcohol, or tobacco smoking, may produce it It occurs in acute and chronic infections, in shock, in some cases of heart failure, in anemia, beriberi, neurocirculatory asthenia and in many other conditions. At night during sleep, the heart rate usually slows However, in hyperthyroidism and in low-grade febrile conditions such as rheumatic fever, the rate at night equals the rate by day.

Symptoms—The patient may complain of palpitations.

Signs.—The neck veins show a systolic collapse. On auscultation of the heart, a tic-toc rhythm may appear, due to the fact that as the heart rate increases, diastole is shortened proportionately more than systole The first sound at the apex may become sharp and accentuated and a pulmonary or apical systolic murmur may appear.

Electrocardiogram.—Sinus rhythm at a rate of more than 100 is present When the rate becomes very rapid, the *P* waves tend to merge with the preceding *T* waves. The *P–R* and *Q–T* intervals shorten as the rate increases (Fig. 63)

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5. Premature Contractions.
   Auricular Premature Contractions, page 337.
   Nodal Premature Contractions, page 338
   Ventricular Premature Contractions, page 339.
6. Paroxysmal Tachycardia.
   Supraventricular Tachycardia page 341.
      Paroxysmal Auricular Tachycardia, page 341.
      Paroxysmal Nodal Tachycardia, page 350.
   Ventricular Tachycardia, page 351.
7. Auricular Flutter and Auricular Fibrillation, page 361.
8. Ventricular Fibrillation, page 354.

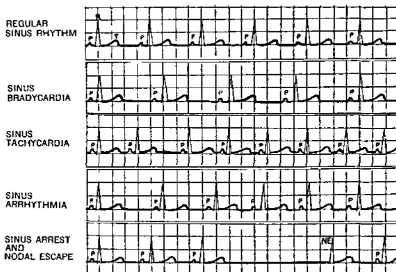


Fig. 63 —Sinus rhythms

SINUS RHYTHMS (Fig. 63)

Regular Sinus Rhythm.—Regular sinus rhythm consists of a regular sequence of characteristic *P* waves, *QRS* complexes, *RS–T* segments and *T* waves, which occur at a regular rate between 60 and 100 per minute. The characteristics of the *P* waves in all forms of sinus rhythm are described on page 85

Sinus Bradycardia.—Sinus bradycardia is arbitrarily described as a sinus rhythm slower than 60 beats per minute. The rate may even be 38 or slower.

Etiology.—Sinus bradycardia is due to increased vagal tone. It occurs in normal people, especially athletes It often occurs during sleep. It can also occur in many abnormal conditions such as intracranial lesions, jaundice, infections such as typhoid, or during convalescence from an infection, in myxedema, in inanition and semistarvation; and during pregnancy. It can also occur as a result of drugs, such as digitalis or quinidine, or from carotid sinus stimulation. It may also occur during acute rheumatic fever.

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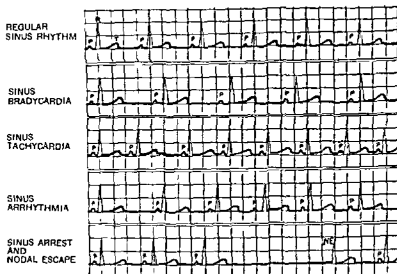


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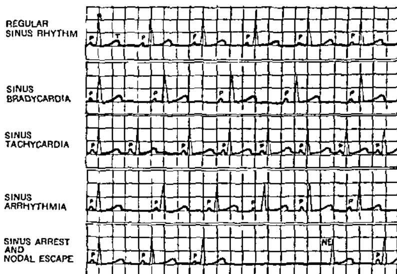


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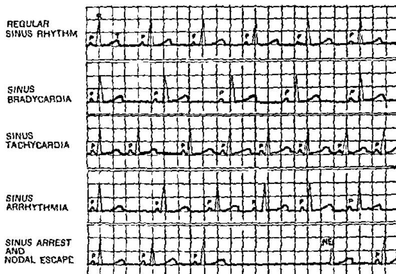


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Diagnosis.—The differentiation of sinus tachycardia from auricular tachycardia is described on page 343

Course and Prognosis.—This depends on the cause of the sinus tachycardia.

Treatment.—The underlying conditions should be treated. If it occurs in nervous but otherwise normal persons, mild sedatives can be prescribed.

Sinus Arrhythmia.—Sinus arrhythmia is a sinus rhythm in which periodic variations in the heart rate occur (Fig 63). These variations are usually related to respiration The heart rate usually increases on inspiration and then slows at the height of inspiration and during expiration. This is known as phasic sinus arrhythmia When the breath is held, the sinus arrhythmia disappears A form of sinus arrhythmia that is not related to respiration, non-phasic sinus arrhythmia, can also occur. Both phasic and non-phasic sinus arrhythmia are aggravated by increasing the depth of breathing

Etiology.—Sinus arrhythmia is a normal phenomenon It is due to variations in vagal tone that occur with respiration. It is very common in children, young adults and old people. It tends to disappear when the heart rate increases Drugs, such as digitalis, may accentuate it. It can also occur during Cheyne-Stokes respiration and during other respiratory abnormalities

Symptoms.—There are usually no symptoms, but if the heart rate slows markedly during the periods of vagal stimulation, the patient may complain of dizziness.

Signs—A characteristic waxing and waning of the heart rate occurs.

Electrocardiogram.—The tracing shows sinus rhythm with a periodic increase and decrease of the heart rate.

Diagnosis.—Sinus arrhythmia can be confused with auricular premature contractions or sinus arrest. However, in both these conditions there is an abrupt slowing of the heart rather than the gradual slowing which occurs in sinus arrhythmia.

Course and Prognosis.—Sinus arrhythmia itself has no clinical significance.

Treatment—No treatment is indicated

Sinus Arrest.—Sinus arrest (sinus block, *s–a* block, sino-auricular block, or cardiac standstill) consists of standstill of the entire heart for one or more beats (Fig 63) Single beats may drop out regularly or irregularly. If alternate beats drop out, the heart rate will decrease one-half and sinus bradycardia occurs Frequently, runs of two or even three dropped beats occur When the period of sinus arrest is long, nodal escape or ventricular escape (see below) may occur

Etiology.—Sinus arrest is due to increased vagal tone. It may occur with a hyperactive carotid sinus. It frequently is produced by digitalis or quinidine or hypopotassemia

Symptoms.—The sudden slowing of the heart may produce dizziness or syncope, and even a convulsive seizure, if the duration of sinus arrest is long

Signs—Sinus arrest is characterized by a regular beating of the heart which is suddenly interrupted by a long pause, after which the heart continues to beat regularly.

Electrocardiogram.—The regular sequence of sinus rhythm is interrupted by a pause which usually is slightly less than twice the interval between two regular beats. This occurs when only one beat drops out. However, the pause of sinus arrest may be much longer than this.

Diagnosis.—The irregular radial pulse that result be simulated by a premature contraction which is f or by the Wenckebach type of *a–v* block, and an el *necessary for diagnosis* However, during the pa waves are noted in the neck veins, whereas in *a–* during the pulse pauses.

Course and Prognosis.—Sinus arrest is usually n sible that it is the cause of sudden death in some p

Treatment.—If sinus arrest is due to digitalis o should be stopped. Atropine or ephedrine will abo

Escape Beats.—When sinus arrest occurs, or w denly slows for any other reason, a normal protect maintain the heart beat, and a new stimulus arise the bundle of His or its branches, or even in the v protective mechanism is known as escape

Electrocardiogram.—An escape beat occurs after than the interval between two regular beats. Wh in the *a–v* node it is called nodal escape, or a nod arises in the branches of the bundle of His, or in t is called ventricular escape or a ventricular escape

A nodal escape beat consists of a QRS complex, wave which appear more or less like the regular co 63) A ventricular escape beat shows a wide aberra aberrant $RS-T$ and T. One escape beat may occu several escape beats at a rate of 60 or less

Diagnosis.—It is practically impossible to mak beats without the electrocardiogram In the elect contractions may resemble escape beats, but a prem *prematurely, that is, before the next regular beat is* which occur after a longer pause than normal

Auricular Standstill.—Auricular standstill occu stops forming stimuli The auricles do not beat b

Etiology.—Cases of so-called auricular standstill result of digitalis or quinidine toxicity and with p may also occur with injury to the sinus node as a

Signs and Symptoms.—*There are no symptoms,* possible on physical examination.

Electrocardiogram.—The tracing shows QRS con and T waves, but no P waves However, there that the P waves are hidden within the QRS as in o (page 322).

Diagnosis—A diagnosis of auricular standstill is tion to the conventional leads, esophageal leads ar taken to rule out auricular activity. (See also pa

Course and Prognosis.—This depends on the etio

Treatment.—Quinidine, or digitalis, if being pr

NODAL RHYTHM (Fig. 64)

In nodal rhythm (*a–v* or atrioventricular nodal rhythm) the *a–v* node is the pacemaker of the heart, and stimulates auricles and ventricles more or less simultaneously.

Etiology.—Nodal rhythm occurs when the sinus node is depressed as a result of vagal stimulation, or due to organic heart disease. It often occurs normally. It may also appear during the course of acute infections, and during acute rheumatic fever and scarlet fever. It may appear after myocardial infarction, during inhalational anesthesia, and can be produced by digitalis, quinidine, and carotid sinus pressure. Atropine may even produce transient nodal rhythm in a normal person. This occurs if atropine releases the vagal control of the *a–v* node more quickly than it releases vagal control of the sinus node.

Symptoms.—There may be no symptoms. However, the patient may complain of a choking or throbbing sensation in the neck. This is due to the fact that when the auricles and ventricles contract simultaneously, the blood from the right auricle cannot enter the ventricle because the tricuspid valve is closed, and thus is propelled into the superior vena cava and the jugular veins, causing a large systolic regurgitant wave in the neck veins.

Signs.—The heart beats regularly at a rate between 30 to 60, but the rate may be faster. A prominent systolic pulsation of the neck veins, synchronous with the radial pulse, is present, and a loud sound can sometimes be heard in the supraclavicular fossa, due to the sudden distention of the internal jugular vein. A systolic pulsation of the liver is occasionally also felt, due to the propulsion of blood from the right auricle into the inferior vena cava and the hepatic veins.

The first heart sound may be accentuated, due to the simultaneous auricular and ventricular systole.

Fluoroscopic and X-Ray Examination.—On fluoroscopic examination, a systolic expansion of the superior vena cava is sometimes visible.

Electrocardiogram.—In nodal rhythm, the stimulus begins in the *a–v* node and spreads normally through the ventricles, so that the *QRS*, *RS–T* and *T* are normal. However, the stimulus spreads from the *a–v* node upward through the auricles, which is opposite to the normal direction of spread. Therefore the shape of the *P* waves change. In the standard leads, $P_{2,3}$ become characteristically downward. P_1 may remain upward. In the augmented unipolar extremity leads, P_{aVR} becomes characteristically upward, and P_{aVF} downward. P_{aVL} is also upward. In the unipolar precordial leads, *P* becomes downward in leads V_{3-6}. (A downward *P* may occur with sinus rhythm if precordial *CF* leads are taken.) The nodal *P* waves may appear before, within, or after the *QRS* complex (Fig. 64, *A*, *B*, *C*). The position of the *P* may be fixed or may vary from beat to beat. When the *P* waves occur simultaneously with the *QRS* complex, they cannot be seen (Fig. 64, *B*) unless esophageal leads are taken. When the *P* waves appear before the *QRS* complex, the *P–R* interval is usually less than 0.1 second.

Diagnosis.—A regular, slow radial pulse in association with large, systolic pulsations in the neck veins is typical of nodal rhythm. (Also see page

150). When nodal rhythm occurs, and the *P* waves are hidden within the *QRS*, the electrocardiogram may simulate auricular fibrillation with fine fibrillatory *f* waves, but the diagnosis of nodal rhythm can be made from the following: (1) The base line between the complexes is perfectly flat This indicates that there is no electrical activity present between the end of *T* and the beginning of *QRS*, (2) Precordial leads $V_{1,2}$ show no *f* waves, (3) If esophageal leads are taken at the auricular level, biphasic *P* waves can be seen within the *QRS*.

This type of nodal rhythm can be differentiated from auricular standstill in the following way. (1) In nodal rhythm, large systolic pulsations occur in the neck veins, whereas in auricular standstill, the neck veins will show a systolic collapse; (2) Esophageal leads will show *P* waves within the *QRS* in nodal rhythm, but not in auricular standstill; (3) Phonocardio-

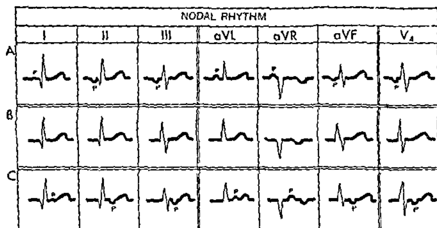


Fig 64 — Nodal rhythm

graphic studies will show additional vibrations superimposed on the first portion of first heart sound, but in auricular standstill, the initial vibrations of the first heart sound are normal.

Course and Prognosis.—This depends on the etiology of the nodal rhythm.

Treatment.—No treatment is usually necessary. However, atropine or ephedrine can abolish it.

WANDERING PACEMAKER

A wandering pacemaker consists of a continual change in the site of stimulus formation from the sinus node to the auricular muscle, to the *a-v* node and back again to the sinus node. When this occurs, the shape of the *P* wave and even the width of the *P–R* interval change from beat to beat It is rare for the nodal *P* waves that occur in a case of wandering pacemaker to appear after the *QRS*.

Etiology.—Wandering pacemaker is due to vagal stimulation. It occurs normally, but may be produced by digitalis, and is seen in acute infections and acute rheumatic fever. It may appear for a few beats after a premature contraction.

Symptoms and Signs.—There are no symptoms, and the diagnosis is made from the electrocardiogram.

Treatment.—No treatment is generally necessary. However, if it occurs in a digitalized patient, the digitalis should be discontinued.

A-V BLOCK (Fig. 65)

A-V block (heart block) exists when conduction of the stimulus from the auricles to the ventricles through the *a–v* node is slowed or blocked. The *a–v* block may be transient, permanent or intermittent. It may be incomplete or complete. The various types frequently pass into one another unless the block is permanent.

Inasmuch as *a–v* block is usually described in terms of its electrocardiographic characteristics, these will be described for each type of *a–v* block, before the clinical features are described.

Incomplete A-V Block.—Incomplete *a–v* block occurs in three forms:

1. **Prolonged P-R Interval (First Degree A-V Block)**.—*Electrocardiogram* (Fig. 65).—In an adult, a *P–R* interval of more than 0.2 second, and in a child, a *P–R* interval of more than 0.18 second is usually considered abnormal. However, a *P–R* interval even as long as 0.24 second has been reported in normal children. An abnormal *P–R* interval may be longer than 0.90 second. When the *P–R* interval is very long, the *P* wave may occur within or before the *T* wave of the preceding beat.

Etiology.—A general discussion of the etiology of all forms of *a–v* block is presented on page 319. However, prolongation of the *P–R* interval has been considered by some cardiologists to be a sign of acute rheumatic carditis. A prolonged *P–R* interval and even more marked forms of *a–v block* often do occur in acute rheumatic fever. However, a prolonged *P–R* interval may occur in normal children, as I mentioned above. Furthermore, it has been shown that atropine shortens a prolonged *P–R* interval in both normal people and in patients with rheumatic fever. This indicates that even in rheumatic fever, the prolonged *P–R* interval is a vagal effect, although this has been questioned by some. The cause of the increased vagal tone in rheumatic fever is unknown. Spontaneous variations of more than 0.04 second in the *P–R* interval may occur from day to day during rheumatic fever, but this can also occur in normal children.

Symptoms.—There are no symptoms.

Signs.—There are no characteristic signs of a prolonged *P–R* interval although the intensity of the first heart sound tends to diminish as the *P–R* interval becomes longer (see page 157).

Diagnosis.—The occurrence of a prolonged *P–R* interval can be suspected if the intensity of the first heart sound in a child decreases. The diagnosis must be confirmed with the electrocardiogram (or jugular vein phlebogram which will show a prolongation of the *a–c* interval).

Course and Prognosis.—This depends on the etiology of the prolonged *P–R* interval

Treatment.—See page 329

2. **Incomplete A-V Block of the Wenckebach Type**.—*Electrocardiogram* (Fig 65).—This type of *a–v* block is due to the fact that each successive stimulus from the auricles finds it more difficult to pass through the *a–v* node. This produces progressive prolongation of the *P–R* interval with each beat Finally, block is complete, the stimulus cannot spread to the ventricles, and a *P* wave appears without a ventricular complex. When the next stimulus reaches the *a–v* node, the node has recovered its ability to conduct, and a short *P–R* interval results. The next beat, however, causes prolongation of the *P–R* interval and the cycle repeats itself

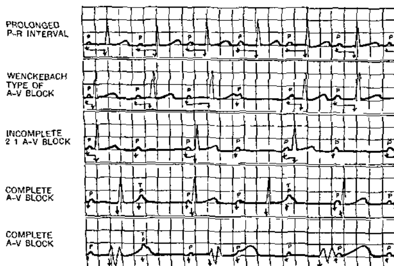


Fig 65 —*A-V* block.

The ventricular rhythm depends on the frequency with which the *a–v* node fails to respond. For example, if every fourth *P* wave is blocked, this can be called a 4:3 type of *a–v* block, because there are four auricular beats and *P* waves to every three ventricular beats and *QRS* complexes With the Wenckebach type of *a–v* block, the ventricular rate is irregular.

Etiology—See page 329

Symptoms—The patient may complain of palpitation due to the irregular heart rate and to the forceful beat after the pause.

Signs.—Auscultation of the heart or palpation of the radial pulse reveals a regular run of the heart beat with frequent pauses (dropped beats). Inspection of the neck veins during these pauses reveals a small venous *a* wave, indicating that the auricles are continuing to beat while the ventricles have stopped Occasionally, on auscultation, a soft and faint heart sound, due to auricular contraction can be heard within the apex.

Etiology.—Wandering pacemaker is due to vagal stimulation. It occurs normally, but may be produced by digitalis, and is seen in acute infections and acute rheumatic fever. It may appear for a few beats after a premature contraction.

Symptoms and Signs.—There are no symptoms, and the diagnosis is made from the electrocardiogram.

Treatment.—No treatment is generally necessary. However, if it occurs in a digitalized patient, the digitalis should be discontinued.

A-V BLOCK (Fig. 65)

A-V block (heart block) exists when conduction of the stimulus from the auricles to the ventricles through the *a–v* node is slowed or blocked. The *a–v* block may be transient, permanent or intermittent. It may be incomplete or complete. The various types frequently pass into one another unless the block is permanent.

Inasmuch as *a–v* block is usually described in terms of its electrocardiographic characteristics, these will be described for each type of *a–v* block, before the clinical features are described.

Incomplete A-V Block.—Incomplete *a–v* block occurs in three forms.

1. **Prolonged P-R Interval (First Degree A-V Block).**—*Electrocardiogram* (Fig. 65).—In an adult, a *P–R* interval of more than 0.2 second, and in a child, a *P–R* interval of more than 0.18 second is usually considered abnormal. However, a *P–R* interval even as long as 0.24 second has been reported in normal children. An abnormal *P–R* interval may be longer than 0.90 second. When the *P–R* interval is very long, the *P* wave may occur within or before the *T* wave of the preceding beat.

Etiology.—A general discussion of the etiology of all forms of *a–v* block is presented on page 319. However, prolongation of the *P–R* interval has been considered by some cardiologists to be a sign of acute rheumatic carditis. A prolonged *P–R* interval and even more marked forms of *a–v* block often do occur in acute rheumatic fever. However, a prolonged *P–R* interval may occur in normal children, as I mentioned above. Furthermore, it has been shown that atropine shortens a prolonged *P–R* interval in both normal people and in patients with rheumatic fever. This indicates that even in rheumatic fever, the prolonged *P–R* interval is a vagal effect, although this has been questioned by some. The cause of the increased vagal tone in rheumatic fever is unknown. Spontaneous variations of more than 0.04 second in the *P–R* interval may occur from day to day during rheumatic fever, but this can also occur in normal children.

Symptoms.—There are no symptoms.

Signs.—There are no characteristic signs of a prolonged *P–R* interval although the intensity of the first heart sound tends to diminish as the *P–R* interval becomes longer (see page 157).

Diagnosis.—The occurrence of a prolonged *P–R* interval can be suspected if the intensity of the first heart sound in a child decreases. The diagnosis must be confirmed with the electrocardiogram (or jugular vein phlebogram which will show a prolongation of the *a–c* interval).

Course and Prognosis.—This depends on the etiology of the prolonged *P–R* interval.

Treatment.—See page 329

2 **Incomplete A-V Block of the Wenckebach Type.**—*Electrocardiogram* (Fig. 65).—This type of *a–v* block is due to the fact that each successive stimulus from the auricles finds it more difficult to pass through the *a–v* node. This produces progressive prolongation of the *P–R* interval with each beat. Finally, block is complete, the stimulus cannot spread to the ventricles, and a *P* wave appears without a ventricular complex. When the next stimulus reaches the *a–v* node, the node has recovered its ability to conduct, and a short *P–R* interval results The next beat, however, causes prolongation of the *P–R* interval and the cycle repeats itself.

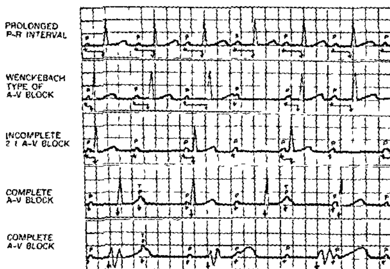


Fig 65.—*A-V* block.

The ventricular rhythm depends on the frequency with which the *a–v* node fails to respond. For example, if every fourth *P* wave is blocked, this can be called a 4:3 type of *a–v* block, because there are four auricular beats and *P* waves to every three ventricular beats and *QRS* complexes. With the Wenckebach type of *a–v* block, the ventricular rate is irregular.

Etiology.—See page 329.

Symptoms.—The patient may complain of palpitation due to the irregular heart rate and to the forceful beat after the pause.

Signs—Auscultation of the heart or palpation of the radial pulse reveals a regular run of the heart beat with frequent pauses (dropped beats). Inspection of the neck veins during these pauses reveals a small venous *a* wave, indicating that the auricles are continuing to beat while the ventricles have stopped. Occasionally, on auscultation, a soft and faint heart sound, due to auricular contraction can be heard within the apex.

Exercise may cause the ventricular rhythm to become normal, even though a–v block persists. For example, if at rest a Wenckebach type 3:2 a–v block is present, and the auricles are beating at a rate of 100, the ventricles have an irregular rate of 66. Exercise may increase the auricular rate to 120, but fewer of the stimuli may be able to penetrate the a–v node and a 2:1 block occurs. The ventricular rate becomes regular but falls to 60

Carotid sinus stimulation, or drugs, such as digitalis, may aggravate the type of a–v block

Diagnosis.—The Wenckebach type of a–v block produces an irregular ventricular rhythm and radial pulse, and must be differentiated from sinus arrest, and from premature contractions. In sinus arrest, the neck veins show no pulsations during the pause in the radial pulse. Auricular premature contractions may be difficult if not impossible to differentiate from the Wenckebach type of a–v block because an auricular premature contraction may not result in a ventricular contraction but can cause a pulsation in the neck veins Similarly, occasional ventricular premature contractions may be too weak to cause a pulse wave to be transmitted to the radial pulse, thus producing a dropped beat at the radial pulse. However, on auscultation of the heart, the premature beat can be heard. This is not pathognomonic of premature contractions because a similar faint heart sound may result from the auricular contraction during the pause in the Wenckebach type of a–v block The diagnosis should therefore be confirmed with the electrocardiogram.

Course and Prognosis.—This depends on the cause of the a–v block.

Treatment —(See page 329.)

3 **Incomplete A-V Block of the 2:1, 3:1, 4:1 Type, etc.**—*Electrocardiogram* (*Fig* 52) —In this form of incomplete a–v block, the a–v node fails to respond to the sinus stimuli at regular intervals, and the ventricular rate is slow and regular. The ventricular rate depends on the frequency with which the a–v node responds. For example, the a–v node can respond to every third auricular beat Thus there would be three auricular beats and P waves to one ventricular beat and QRS complex. In other words, a 3:1 a–v block would be present. The P waves that are followed by QRS complexes always show a constant P–R interval.

Etiology.—See page 329

Symptoms —The slow, forceful ventricular rate may cause palpitation.

Signs —The ventricular rate and the radial pulse are slow and regular. The neck veins not only show a systolic collapse, coincident with the radial pulse, but show small pulsations of auricular origin at a rate of two, or three, or four or more times faster than the radial pulse rate, indicating that a–v block is present (Fig. 37, page 150).

On auscultation, auricular sounds may be heard during diastole, in addition to the regular heart sounds.

Diagnosis.—The differentiation of this type of incomplete a–v block from complete a–v block, sinus bradycardia or nodal rhythm on physical examination is described on page 150. Electrocardiographic differentiation from complete a–v block is described on page 328.

Course and Prognosis.—This depends on the etiology of the block.

Treatment —See page 329.

Complete A-V Block.—*Electrocardiogram* (Fig. 65) —When complete *a–v* block is present, all of the auricular stimuli are blocked at the *a–v* node. Consequently, in order for the ventricles to beat, a pacemaker arises in some portion of the *a–v* node that can still function, or in the bundle of His or its branches, or in the Purkinje network or even in some region of the ventricular muscle, and the ventricles continue to beat at a slow regular rate. This independent ventricular rhythm is known as *idioventricular rhythm*.

When the ventricles are stimulated by the *a–v* node, the *QRS* complexes, *RS–T* segment and *T* waves are more or less normal (Fig 65, *D*). When the ventricles are stimulated by a pacemaker in one of the branches of the bundle of His or in the ventricular muscle, the ventricular complexes become wide and aberrant and often resemble the patterns of right or left bundle branch block (Fig 65, *E*). Because of this, a diagnosis of bundle branch block should not be made when complete *a–v* block is present.

The ventricles usually beat at a slow regular rate between 30 and 60, but the rate may be as low as 12, and rarely faster than 60. When the stimulus arises in the *a–v* node and the ventricular complexes are normal, the rate is usually faster than when the stimulus arises in one of the branches of the bundle of His or in the Purkinje network or in the ventricular muscle.

Complete a–v block is therefore recognized by the presence of P waves which appear regularly, and R waves which also appear regularly but at a much slower rate. There is no constant *P–R* interval, and the presence of a *P* wave closely followed by a *QRS* complex is coincidental and is not due to the spread of the stimulus from auricles to ventricles. Rarely, the ventricular rate is irregular with complete *a–v* block. This occurs if the location of the idoventricular pacemaker shifts, of if the ventricles temporarily cease to beat, or if ventricular premature contractions occur.

Etiology.—See page 329.

Symptoms.—The patient usually does not have symptoms so long as the ventricular rhythm is regular. However, he may be conscious of the slow forceful beating of the heart, and when the ventricular rate is very slow, may complain of dizziness. In addition, the Adams-Stokes syndrome (page 328) may appear.

Signs.—The slow, regular ventricular rate has already been mentioned. The auricles are usually stimulated in a normal way from the sinus node at a rate of 70 or more. (In some cases of complete *a–v* block, the auricles may show auricular fibrillation or flutter.) Thus the radial pulse is slow and full, whereas the neck veins not only show the normal systolic collapse coincident with the radial pulse, but show small auricular pulsations during the diastolic pauses, just as occurs in some cases of incomplete *a–v* block. However, since the auricles and ventricles are beating completely independently of each other when complete *a–v* block is present, auricles and ventricles may occasionally contract simultaneously. When this happens, a large systolic wave appears in the neck veins (see page 151).

The slow ventricular rate causes the stroke volume to increase, and the forceful ejection of blood from the ventricles causes the systolic blood pressure to rise even above 150 mm. The long diastolic period allows the diastolic pressure to fall, so that the pulse pressure may be 80 or 90 mm.

The first heart sound varies in intensity from beat to beat, depending on the varying positions of the *a–v* valves at the onset of ventricular systole Additional heart sounds, produced by the contracting auricles may also appear, and give the appearance of a gallop rhythm. When auricles and ventricles contract almost simultaneously, a loud sharp, first heart sound (cannon sound) may appear (see page 158). Contraction of the auricles at the time of closure of the semilunar valves may accentuate the second heart sound

Exercise, amyl nitrite, or atropine may increase the auricular rate but usually has little or no effect on the ventricular rate.

Diagnosis—The differentiation of complete *a–v* block from incomplete *a–v* block of the 2:1, 3:1, *etc.*, type, from nodal rhythm and from sinus bradycardia by means of physical examination is described on page 150. The absence of a constant *P–R* interval differentiates complete *a–v* block in the electrocardiogram from incomplete *a–v* block where the ventricular rate is also regular.

The Adams-Stokes Syndrome (Morgagni-Adams-Stokes or Stokes-Adams) Syndrome.—*This consists of attacks of syncope which may be followed by convulsive movements* The attacks occur in cases of complete *a–v* block when the ventricular rate suddenly slows, or when the ventricles stop *beating effectively for any length of time. This may occur as a result of* cardiac standstill where both the auricles and ventricles stop beating and the electrocardiogram shows a long pause; or from ventricular standstill, where the auricles continue to beat but the ventricles cease, and the electrocardiogram shows *P* waves but no ventricular complexes for a long period; or from transient ventricular fibrillation.

If the attack lasts as long as a second or two, the patient may experience a sudden clouding of consciousness which disappears almost immediately. If the attack lasts five or ten seconds, the patient loses consciousness and will fall to the ground if he has been standing. The pulse is absent, a deathly pallor appears, and stertorous respirations may develop If the attack continues, cyanosis and a convulsive seizure appears in about sixteen seconds. When the attack ends and the heart begins to beat normally, a pink flush spreads over the patient's body The attacks usually last less than a minute, and may vary in frequency from one or less a month to an attack every few minutes Cardiac asystole which is followed by recovery may last as long as one minute or longer. (In cases of cardiac arrest from anesthesia during surgical operations, recovery has occurred even after cardiac asystole of twenty or more minutes—see page 763)

The attacks may occur suddenly and without warning while the patient is working or walking or at rest. In patients with complete *a–v* block who develop attacks of ventricular fibrillation, the attack often starts with a run of premature ventricular contractions which may serve as a warning *to the patient. When the attack is due to cardiac standstill,* the neck vein pulsations disappear, but if the attack is due to ventricular standstill, the neck vein pulsations due to auricular systole continue during the attack. This may also occur during a run of ventricular fibrillation. The cerebral signs of the Adams-Stokes syndrome are due to cerebral anoxia resulting from the cardiac asystole.

The Adams-Stokes syndrome may also occur in patients who develop paroxysmal tachycardia (either auricular, nodal, or ventricular, or auricular flutter or fibrillation with a rapid ventricular rate) In such cases, the period of diastole becomes so short that the stroke volume and cardiac output fall greatly, producing cerebral anoxia

Patients with aortic stenosis also have syncopal attacks, the exact mechanism of which is unknown In some patients, an attack of angina pectoris or acute myocardial infarction, or dissecting aneurism of the aorta, or a pulmonary embolus may start with syncope rather than pain The syncope in dissecting aneurism may be due to mechanical stimulation of the aortic depressor nerve by the dissecting column of blood

The occurrence of Cheyne-Stokes respiration during the Adams-Stokes syndrome is described on page 152.

The Etiology of A-V Block.—When the *a–v* node is clamped in an experimental animal, *a–v* block develops in the following stages: prolonged *P–R* interval, then the Wenckebach type of *a–v* block, then a 2:1, 3:1, *etc*, type of *a–v* block, and finally complete *a–v* block Clinically, however this sequence does not necessarily occur

A–V block, complete or incomplete, can occur clinically in the following ways.

1 As a result of vagal stimulation. Vagal tone can be enhanced by drugs, such as digitalis, or as a result of carotid sinus stimulation, or even changes in posture, or vagovagal reflexes originating in the gastrointestinal or respiratory tract The *a–v* block that occurs in hyperthyroidism, acute rheumatic fever, scarlet fever, mumps, German measles, and other infectious conditions is probably also due to an increased vagal tone

2 As a result of drugs, and toxins, such as diphtheria toxin, digitalis, quinidine, morphine, *etc*, that affect the *a–v* node directly The *a–v* block that occasionally occurs in uremia can also be explained in this way *A–V* block can also develop during an attack of paroxysmal auricular tachycardia In such cases, the rapid heart rate causes fatigue and refractoriness of the *a–v* node, which disappear when the heart rate slows

3 As a result of pathological conditions that injure the *a–v* node, such as syphilitic gummata of the interventricular septum, rheumatic carditis, bacterial endocarditis, congenital lesions of the interauricular or interventricular septum (page 393), myocardial infarction, coronary artery disease, calcific disease of the aortic valve with extension of the calcification into the interventricular septum, *etc.*

Course and Prognosis of A-V Block.—This depends on the etiology of the *a–v* block. Usually *a–v* block, even if complete, is not serious unless the Adams-Stokes syndrome occurs. Yet I have known patients with the Adams-Stokes syndrome due to ventricular fibrillation to live many years after the seizures occurred

Treatment of A-V Block.—*A–V* block, even if complete, does not necessarily require treatment If due to drugs, the drug should be discontinued If due to acute myocardial infarction, I usually prescribe 0 4 mg. ($\frac{1}{150}$ grain) of atropine several times a day orally

When the patient is suffering from Adams-Stokes seizures, 0.4 mg. ($\frac{1}{150}$ grain) of atropine, or 15 to 30 mg ($\frac{1}{4}$ to $\frac{1}{2}$ grain) ephedrine, or 30 to 60 mg

($\frac{1}{2}$ to 1 grain) of paredrine can be given several times a day prophylactically. Isuprel (isopropylarterenol) can be given sublingually three or four times a day. It is supplied in tablets of 10 and 15 mg. strength. The atropine-like drug, pro-banthine, can also be used (one 15 mg. tablet, three or four times a day).

Desiccated thyroid hormone, in a daily dose of 15 to 60 mg. ($\frac{1}{4}$ to 1 grain) has also been used prophylactically.

Aminophylline either orally (page 254) or in suppository form may also be valuable.

During the attack, 0.5 cc. epinephrine ($\frac{1}{1000}$) can be injected subcutaneously, and in cases where death seems imminent, 0.5 cc. epinephrine can be injected directly into the heart, using a $2\frac{1}{2}$ inch needle.

External electric stimulation of the heart has also been used.

When the attacks are due to ventricular fibrillation, the prophylactic therapy described above can also be used, but may be ineffective. In such cases, small doses of quinidine, 0.2 gram (3 grains) several times a day, or even smaller doses, can be tried. However, one should remember that in general, quinidine is contraindicated when *a–v* block is present because it may produce cardiac arrest. Procaine amide is also contraindicated.

During an attack of ventricular fibrillation, epinephrine is contraindicated. *In such cases, the intracardiac injection of 5 to 10 cc. of a 1 per cent procaine solution may be of value if death appears imminent.*

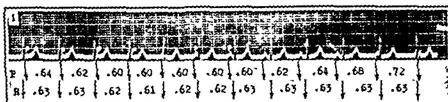
Although quinidine is ordinarily contraindicated in cases of *a–v* block, digitalis can be used if heart failure is present, and I have occasionally seen *a–v* block disappear and sinus rhythm return after digitalization in such cases. However, heart failure is comparatively infrequent in cases of complete *a–v* block.

A–V DISSOCIATION

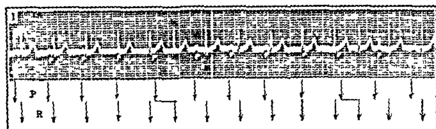
A–V dissociation exists when the auricles and ventricles beat independently, the ventricular rate being the same or slightly faster than the auricular rate. It represents an attempt of the ventricles to escape from the depressive effect of vagal stimulation. *A–V* dissociation may be complete or incomplete. (Some cardiologists use the term "*a–v* dissociation" synonymously with "*a–v* block," but there are important differences between the two conditions.)

In the arrhythmias that I have described already, either the sinus node or some other neuromuscular tissue is the pacemaker of the heart. In *a–v* dissociation, there are two pacemakers competing with each other for dominance. The sinus node stimulates the auricles, and the *a–v* node stimulates the ventricles more or less simultaneously so that when the stimulus from the sinus node reaches the *a–v* node, the *a–v* node is still refractory as a result of its own previous stimulus, and the sinus stimulus is not *able to spread through the ventricles (complete a–v dissociation, Fig. 53, A).* To some extent, this condition is similar to what happens in *a–v* block. However, there is an important difference between the two conditions because in *a–v* dissociation, when a sinus stimulus reaches the *a–v* node early, it is able to penetrate it and cause the ventricles to beat prematurely. This is known as incomplete *a–v* dissociation, or *a–v* dissociation with interference (Fig. 66, *B*).

Both complete and incomplete *a–v* dissociation can occur normally. However, *a–v* dissociation also occurs after myocardial infarction, during acute rheumatic fever, pneumonia, diphtheria and other infections, as a result of digitalis, quinidine, etc.



A



B

FIG 66.—*A*, Complete *a–v* dissociation. Notice that auricles and ventricles are beating independently of each other and that the ventricular rate tends to be slightly faster than the auricular

B, Incomplete *a–v* dissociation, or *a–v* dissociation with interference Notice that occasional auricular stimuli penetrate the *a–v* node and cause the ventricles to beat irregularly. (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed , 1953)

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Chapter 19

PREMATURE CONTRACTIONS, AND PAROXYSMAL TACHYCARDIA

PREMATURE CONTRACTIONS

THE term premature contraction, premature beat, premature systole or extra systole indicates that the auricles or ventricles are stimulated prematurely, that is, before the next regular beat is due, from an ectopic focus or ectopic foci located in the auricles or ventricles These premature contractions are called auricular premature contractions when they arise in some portion of the auricular muscle Premature contractions can arise in the sinus node (sinus premature contractions), but it is almost impossible to differentiate them from other auricular premature contractions. Nodal premature contractions arise in the *a–v* node Ventricular premature contractions arise in one of the branches of the bundle of His, the Purkinje network, or in the ventricular muscle.

Premature contractions may occur infrequently, or at regular intervals, such as every second beat, or every third beat, *etc*, producing coupling (see page 340) They may occur as single, isolated, premature beats or in runs of several successive premature beats A run of several successive premature beats is known as a paroxysmal tachycardia (page 341)

Etiology —Premature contractions occur when a region of the heart becomes irritated. The cause of this is unknown in most cases. For example, premature beats may occur spontaneously in normal people on excitement or breath-holding Tea, coffee, tobacco smoking, and alcohol may also induce premature beats in susceptible normal persons Drugs, such as digitalis, can also produce premature contractions, possibly by altering the electrolyte balance of heart muscles, and causing a withdrawal of potassium from the muscle Premature beats can also occur as a result of direct mechanical stimulation of the heart, or manipulation of the intrathoracic nerves, as occurs during surgical procedures on the heart or thoracic organs

Auricular premature contractions may be the precursor of auricular tachycardia or auricular fibrillation Ventricular premature contractions may be the precursor of ventricular tachycardia, and sometimes ventricular fibrillation

A rare type of premature contraction has been explained by the theory of parasystole, which assumes that an ectopic focus is located in either the auricles or ventricles, producing stimuli at a regular rate. However, only some of these ectopic stimuli are able to spread through the heart to form premature contractions.

In adults, premature ventricular contractions are more frequent than premature auricular contractions; in children, the reverse occurs.

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Etiology.—Premature contractions occur when a region of the heart becomes irritated. The cause of this is unknown in most cases For example, premature beats may occur spontaneously in normal people on excitement or breath-holding Tea, coffee, tobacco smoking, and alcohol may also induce premature beats in susceptible normal persons Drugs, such as digitalis, can also produce premature contractions, possibly by altering the electrolyte balance of heart muscles, and causing a withdrawal of potassium from the muscle Premature beats can also occur as a result of direct mechanical stimulation of the heart, or manipulation of the intrathoracic nerves, as occurs during surgical procedures on the heart or thoracic organs

Auricular premature contractions may be the precursor of auricular tachycardia or auricular fibrillation. Ventricular premature contractions may be the precursor of ventricular tachycardia, and sometimes ventricular fibrillation.

A rare type of premature contraction has been explained by the theory of parasystole, which assumes that an ectopic focus is located in either the auricles or ventricles, producing stimuli at a regular rate However, only some of these ectopic stimuli are able to spread through the heart to form premature contractions

In adults, premature ventricular contractions are more frequent than premature auricular contractions; in children, the reverse occurs.

Symptoms.—Premature beats are often symptomless However, they may produce a disagreeable sensation in the chest, or palpitation. Occasionally there is a sense of fullness in the neck, due to blood regurgitating from the right auricle into the neck veins. This occurs, for example, after a ventricular or nodal premature contraction, if the auricles contract while the ventricles are still in systole and the tricuspid valve is closed. It can also occur after a premature auricular contraction which occurs during ventricular systole. (Such a premature auricular contraction does not cause the ventricles to contract because the ventricles are already in systole, and it is known as a blocked auricular premature contraction.) A run of several premature contractions may produce a feeling of dizziness

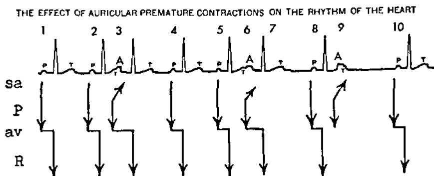


Fig. 67 —Diagram showing the effect of auricular premature contractions, *A*, on the rhythm of the heart

The arrows indicate the direction in which the stimuli spread through the heart *sa*, Sinus node, *P*, represents the spread of the stimulus through the auricles; *av*, *a–v* node, *R*, represents the spread of the stimulus through the ventricles The horizontal line connecting the upper and lower rows of arrows represents the duration of the *P–R* interval

(1) and (2) show regular sinus rhythm

(3) Is an auricular premature contraction It travels through the auricles, and penetrates both the sinus node and the *a–v* node The ventricles beat prematurely The prematurely stimulated sinus node forms another stimulus and the next heart *beat is* normal However, the sum of the *P–P* intervals immediately before and after the auricular premature contraction is *less than* the sum of two regular *P–P* intervals, and the interval or pause that follows the auricular premature contraction is called *not fully compensatory* *Most auricular premature contractions are followed by a pause that is not fully compensatory*

(4) and (5) show regular sinus rhythm

(6) Is another auricular premature contraction It spreads to the *a–v* node and causes the ventricles to beat prematurely However, it does not penetrate the sinus node, and does not disturb stimulus formation of the sinus node. However, when regular sinus stimulus (7) is formed it cannot spread through the auricles because they are still refractory from the last beat Sinus stimulus (7) is not recorded in the electrocardiogram, and, after a pause, regular sinus beat (8) occurs One reason why auricular premature contraction (6) did not penetrate the sinus node is that the node may have been shielded from the action of premature stimuli by means of unidirectional block that allows a stimulus to pass out of the sinus node but not to enter Such a block is known as *entrance or protection block* Since sinus stimulus (7) was not prematurely discharged by the auricular premature contraction, the sum of the *P–P* intervals immediately before and after the auricular premature contraction equals the sum of two regular *P–P* intervals, and the interval or pause after this auricular premature contraction is called *fully compensatory*

(9) Is another auricular premature contraction. It spreads through the auricles and penetrates the sinus node but it reaches the *a–v* node while it is still refractory. The ventricles therefore do not beat and the auricular premature contraction is blocked After a pause, regular sinus beat (10) occurs

Signs.—Auscultation of the heart will reveal the premature beat. The first sound of the premature beat (either an auricular or ventricular premature contraction) is usually louder than the regular first heart sound. On palpation of the radial pulse, the premature beat is usually felt. Occasionally, the premature beat occurs when there is but little blood in the heart and the resulting contraction of the heart may be too feeble to open the semilunar valves so that no blood is expelled from the ventricles (frustrane contraction) In such a case, the radial pulse merely records a long pause.

Nodal and ventricular premature contractions and blocked auricular premature contractions may produce a large systolic pulse wave in the neck veins, due to simultaneous auricular and ventricular systole.

Electrocardiogram.—The various types of premature contractions can be readily differentiated in the electrocardiogram:

Auricular Premature Contractions (Fig. 67).—An auricular premature contraction has the following characteristics.

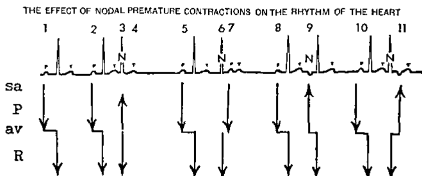


FIG 68—Diagram showing the effect of nodal premature contractions, *N*, on the rhythm of the heart See caption of figure 67

(1) and (2) show regular sinus rhythm

(3) Is a nodal premature contraction The premature stimulus spreads through ventricles and auricles Entrance block prevents it from penetrating the sinus node Shortly after this, regular sinus stimulus (4) occurs However, this stimulus does not spread through the auricles which are now refractory It is not noted on the electrocardiogram

After a pause, the next regular sinus stimulus (5) occurs, and the auricles and ventricles again beat normally The sum of the *P-P* intervals immediately before and after the nodal premature contraction is equal to the sum of two regular *P-P* intervals, because the nodal premature contraction did not disturb stimulus formation in the sinus node The pause that follows this nodal premature contraction is therefore fully compensatory *Most nodal premature contractions are followed by a fully compensatory pause*

(6) Is a nodal premature contraction which does not spread through the auricles because of retrograde block at the a-v node The ventricles beat prematurely, and a moment later, regular sinus stimulus (7) occurs and spreads through the auricles, forming a sinus *P* wave within the *QRS* This stimulus does not penetrate the *a-v* node which is refractory Occasionally part of the *P* lies immediately before the *QRS* Occasionally the *P* occurs after the *QRS* After a compensatory pause, regular sinus beat (8) occurs

(9) Is a nodal premature contraction that spreads through the auricles and ventricles. It resembles nodal premature contraction (3) but here the stimulus spreads through the auricles sooner than it spreads through the ventricles A premature nodal *P* therefore precedes the *QRS* This nodal premature contraction penetrates the sinus node and after a pause that is not fully compensatory regular sinus beat (10) occurs.

(11) Is another nodal premature contraction Here the stimulus spreads through the ventricles sooner than it spreads through the auricles, and the premature nodal *P* appears after the *QRS*

1 A premature P wave is present Because it is premature it often is superimposed on the T wave of the preceding beat. The premature P is usually followed by a ventricular complex, but occasionally is not (blocked auricular contraction).

2. The premature P may or may not be aberrant in shape. That is, it may or may not resemble the other P waves in the lead When multiple auricular premature contractions arise from a single focus, they are similar in shape in any lead When they arise from varying foci, they vary in shape in any lead

3 The P–R interval of the auricular premature contraction is usually longer than the other P–R intervals in the tracing, but it may be the same or shorter

4. The ventricular complex that follows usually resembles the other ventricular complexes in the lead, but abnormalities of QRS, RS–T or T may appear

Nodal Premature Contractions (Fig 68) —Two types of nodal premature contractions may occur.

1 A premature nodal P (page 322), followed by a QRS, RS–T and T.

2. A premature, normal-appearing QRS, RS–T and T, without a P The nodal P in such a case is hidden within the QRS. Occasionally a nodal (or sinus) P follows the QRS and is superimposed on the RS–T segment.

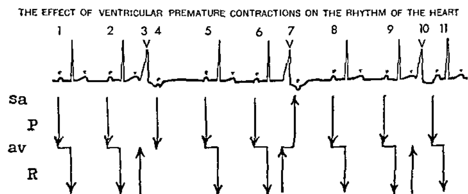


FIG 69 —Diagram showing the effect of ventricular premature contractions, V, on the rhythm of the heart See caption of figure 67.

(1) and (2) show regular sinus rhythm

(3) Is a ventricular premature contraction The ventricles beat prematurely, but unidirectional block at the a–v node prevents the stimulus from spreading to the auricles While the ventricles are in a state of contraction and therefore refractory, the next regular sinus stimulus (4) causes the auricles to beat. However, this stimulus cannot penetrate the refractory a–v node After a pause, regular sinus beat (5) occurs The sum of the R–R intervals immediately before and after the ventricular premature contraction is equal to the sum of two regular R–R intervals because the ventricular premature contraction did not disturb the regular sinus rhythm, and the pause that follows ventricular premature contraction (3) is called *fully compensatory* *Most ventricular premature contractions are followed by a fully compensatory pause*

(6) Shows regular sinus rhythm

(7) Is another ventricular premature contraction Here the premature stimulus penetrates the a–v node and spreads upwards through the auricles and prematurely discharges the sinus node The pause that follows ventricular premature contraction (7) is therefore not fully compensatory

(8) and (9) show regular sinus rhythm

(10) Is called an *interpolated* ventricular premature contraction because it does not disturb the regular sinus rhythm and is followed by regular sinus beat (11).

Ventricular Premature Contractions (Fig. 69) —These are characterized by:

1. A premature *QRS* complex which is 0.12 second or more wide, aberrant, notched or slurred. It is associated with a *T* wave that usually points in a direction opposite to the main deflection of the *QRS*. Multiple ventricular premature contractions from one focus show the same shape in any lead, from varying foci, different shapes.
2. The premature *QRS* is not preceded by a *P* wave.

The Diagnosis of Premature Contractions.—The only accurate method of diagnosing premature contractions is with the electrocardiogram. Clinically, auricular premature contractions can sometimes be differentiated from ventricular or nodal premature contractions by timing the jugular vein pulsations with the radial pulse. An auricular premature contraction will cause a small jugular pulsation just before the premature beat is felt in the radial pulse A ventricular or nodal premature contraction will usually cause a large jugular pulsation coincident with the radial pulse, due to the fact that auricular systole occurs while the ventricles are still contracted

Another method of differentiating auricular from ventricular premature contractions that has been described is to determine whether the pause that follows the premature contraction is fully compensatory or not, because ventricular (and nodal) premature contractions are usually followed by a fully compensatory pause, whereas auricular premature contractions are usually followed by a shorter pause

A fully compensatory pause is produced by a ventricular premature contraction in the following way: When the ventricular premature contraction occurs, the stimulus usually does not spread upward through the *a–v* node to the auricles, so that the auricular rhythm is not disturbed, and the next auricular beat occurs on time However, it cannot spread through the ventricles which are still refractory as a result of the premature beat Thus the regular ventricular beat does not occur until the sinus node and the auricles are again stimulated. The premature beat is therefore followed by a long interval or pause, which is called fully compensatory because the sum of the intervals preceding and following the premature beat equals two normal heart cycles

An auricular premature contraction on the other hand, usually discharges the sinus node as well as the ventricles prematurely so that the next sinus stimulus and heart beat occur comparatively soon after the premature beat, and the sum of the intervals preceding and following the auricular premature contraction is less than the sum of two normal cycles. Thus the pause after an auricular premature contraction is not fully compensatory. However, ventricular and nodal premature contractions may be followed by a pause that is not fully compensatory, and an auricular premature contraction may be followed by a fully compensatory pause Actually it is difficult to make the distinction between a fully compensatory pause and one that is not, on physical examination, although it can be done with ease in the electrocardiogram (Figs 67, 68, 69)

Auricular fibrillation can simulate premature contractions because of the irregular ventricular rhythm that is usually present with auricular fibrillation However, if a systolic collapse of the neck veins is present, this is sufficient to rule out auricular fibrillation even if the pulse is grossly irregu-

lar. The systolic collapse of the neck veins merely indicates that some form of sinus rhythm is present.

Palpation of the radial pulse, or preferably the apical impulse, alone can often differentiate premature contractions from auricular fibrillation, because if premature contractions are present, the pause follows two beats in quick succession (a normal beat and the premature beat), whereas in auricular fibrillation, the rhythm of the heart is totally irregular and long pauses will occur which are not preceded by two beats in quick succession. However, one should remember that auricular fibrillation and premature beats may occur at the same time.

It has been stated that after exercise, ventricular premature contractions tend to disappear, making the heart regular, whereas exercise tends to make the heart more irregular if auricular fibrillation is present. However, exercise can cause multiple premature auricular or ventricular contractions to appear.

When premature contractions occur every second beat, they produce what has been called a bigeminal rhythm (pulsus bigeminus or bigeminy) consisting of a sequence of two beats followed by a pause. If the premature contractions occur every third beat, a triple rhythm (pulsus trigeminus or trigeminy) occurs, and if the premature contraction occurs every fourth beat, a quadruple rhythm (pulsus quadrigeminus) occurs. The presence of such coupled pulse rhythms or coupling, however, is not necessarily a sign that premature contractions (auricular or ventricular) are present, because coupling can occur with *a–v* block, sinus arrest, and in other ways. Similarly, although it is common for digitalis to produce ventricular premature contractions occurring every second or third beat as a toxic manifestation, ventricular premature contractions may occur with such rhythms even though digitalis has not been administered.

The electrocardiogram sometimes gives information which enables one to determine whether premature contractions are serious or not, because premature contractions from varying foci usually occur in patients with organic heart disease, whereas premature contractions from a single focus may or may not be significant. However, during surgical anesthesia premature contractions from varying foci may occur in persons with normal hearts.

Pulsus alternans can also simulate premature contractions (see page 142).

Course and Prognosis.—This depends on the etiology of the premature contractions. In most instances they are completely innocuous. However, premature contractions from varying foci usually occur in patients with serious heart disease, and premature ventricular contractions produced by digitalis toxicity may be a precursor of ventricular tachycardia or fatal ventricular fibrillation.

Treatment.—In most cases, premature contractions require no drug therapy. However, the patient should be reassured and told that premature beats do not signify heart disease. If some factor, such as tobacco, alcohol, coffee or tea, is believed responsible, it should be eliminated. Mild sedatives can also be prescribed.

If the premature contractions prove particularly annoying, potassium salts orally may be helpful in causing their disappearance. Potassium

chloride (or citrate, acetate, *etc.*) can be prescribed in the form of a 25 per cent solution, and a total of 5 to 10 grams daily can be given. The following prescription can be used:

℞ Potassium chloride 30
Aq. menthæ piperitæ 120.
(peppermint water)
S One teaspoon (1 gram) as indicated.

Potassium salts are particularly effective if the premature contractions are due to digitalis toxicity. Potassium salts can also be given rectally in the form of a 25 per cent solution, and even intravenously (see page 717). However, potassium should be used cautiously in the presence of renal damage or dehydration where the blood potassium level is elevated.

If potassium is ineffective, the patient can be digitalized (page 258) or placed on quinidine, 0.4 gram (6 grains) several times a day. Procaine amide hydrochloride (page 353) has also been used orally for ventricular premature contractions.

PAROXYSMAL TACHYCARDIA

The clinical features of the various forms of paroxysmal tachycardia are very similar, and classification is usually made on the basis of the electrocardiographic patterns. On this basis, paroxysmal tachycardia can be divided into two main groups, supraventricular tachycardia, and ventricular tachycardia.

SUPRAVENTRICULAR TACHYCARDIA

Supraventricular tachycardia actually consists of only auricular tachycardia and nodal tachycardia. However, the term is often used to include attacks due to paroxysmal auricular flutter or auricular fibrillation with a rapid ventricular rate, because it is sometimes impossible to determine the auricular rhythm exactly until the heart slows. The term "supraventricular tachycardia" is justifiable in such cases of auricular flutter or fibrillation because in these conditions, as well as in auricular and nodal tachycardia, the stimulus spreads through the ventricles in a normal way regardless of the auricular rhythm. Clinically it is important to determine whether the tachycardia is supraventricular or ventricular because the etiology, prognosis and treatment of the two types are different.

A supraventricular tachycardia is recognized in the electrocardiogram by a rapid heart rate, usually above 140, questionable or absent P waves, and more or less normal ventricular complexes.

Auricular Tachycardia.—*Electrocardiogram* (Figs. 70 and 71).—Auricular tachycardia is produced by a run of successive auricular premature contractions, which may arise from a single focus or from varying foci. Auricular tachycardia shows the following characteristics in the electrocardiogram:

1. The heart rate is rapid, usually more than 140 per minute. However, the rate can vary from 100 or less to 300 or more a minute.

ever, most cases of auricular tachycardia do not respond to deep inspiration or exercise, and when carotid sinus pressure or other forms of vagal stimulation are effective, the tachycardia usually abruptly ceases, and a slow sinus rhythm returns However, in some cases of auricular tachycardia, carotid sinus pressure may cause momentary slowing of the heart rate just as occurs in sinus tachycardia.

3 A sinus tachycardia usually has a slow and gradual onset and gradually disappears, whereas auricular tachycardia usually begins and ends abruptly. However, this does not always happen.

4 Examination of the neck veins is often helpful. In sinus tachycardia, systolic collapse of the neck veins is usually present, whereas in auricular tachycardia, systolic pulsations of the neck veins are usually present, for reasons described on page 343.

5. The best way of distinguishing auricular tachycardia from sinus tachycardia is to compare the shape of the *P* waves before or after an attack with the *P* waves during an attack. In sinus tachycardia, the *P* waves remain unchanged. In auricular tachycardia, aberration of the *P* and *P–R* interval usually occurs.

Differentiation of Auricular Tachycardia From Nodal Tachycardia.—This can be done only with the electrocardiogram, and even this may be impossible if nodal *P* waves are not present. Nodal tachycardia produces large systolic neck vein pulsations because auricles and ventricles contract more or less simultaneously, but this often also occurs with auricular tachycardia (page 343).

Differentiation of Auricular Tachycardia From Ventricular Tachycardia.—It has been frequently stated that auricular tachycardia can be differentiated from ventricular tachycardia clinically because the ventricular rate in auricular tachycardia is extremely regular, whereas slight irregularities of the ventricular rate occur from moment to moment in ventricular tachycardia However, as I pointed out above this is not necessarily so. The only method of differentiating auricular from ventricular tachycardia is by means of the electrocardiogram, because wide aberrant *QRS* complexes are present in ventricular tachycardia, whereas the *QRS* is more or less normal in auricular tachycardia However, if auricular tachycardia occurs in a patient who has bundle branch block, or the Wolff-Parkinson-White syndrome, the tracing may resemble a ventricular tachycardia, and differentiation may be impossible until the tachycardia stops, and sinus rhythm with bundle branch block or aberrant ventricular complexes persists in the tracing.

The differentiation of auricular tachycardia from auricular flutter is described on page 363, and the differentiation from auricular fibrillation on page 151.

Course and Prognosis.—Attacks may last a few seconds or minutes and disappear spontaneously. However, it is not uncommon for attacks to last several hours, and in rare cases, for days or even weeks or longer. Heart failure usually does not develop even in long-lasting attacks, unless organic heart disease is present. The frequency of the attacks may vary from several times a day, to one a year or less, and there may be long intervals of months or years when the patient is free from attacks The condi-

tion is usually benign However, if it occurs in cases of acute myocardial infarction or organic heart disease, fatal shock or heart failure may result.

In this connection, one should remember that after an attack of paroxysmal tachycardia (supraventricular or ventricular) abnormal *T* waves that simulate the patterns of myocardial infarction may appear and last for several weeks The exact cause of these *T* wave changes is unknown, but may be related to a loss of potassium from the fatigued heart muscle

Treatment —The attack of tachycardia can usually be stopped with one of the following measures:

A. Measures Which Increase Vagal tone·—1. *Carotid Sinus Pressure.*—The simplest way of increasing vagal tone is by means of carotid sinus pressure. The technic of carotid sinus pressure is described on page 258 Pressure should be done first on the right side, then on the left side, and then on both sides simultaneously if necessary, for fifteen to twenty seconds When carotid sinus pressure is effective, a sudden and abrupt slowing of the heart rate occurs. At this point, the carotid sinus pressure should be discontinued to prevent cardiac asystole In addition, the patient should be recumbent or semirecumbent, in case syncope occurs. One should remember that even if carotid pressure is unsuccessful, it can be tried again, often with success, if other measures to stop the tachycardia are ineffective (see page 349).

2 *Eyeball Pressure* —I have not found this as effective as carotid sinus pressure. The patient is directed to look downward and to close his eyes Pressure is then made on the closed eyes with the fingers, just below the supraorbital ridge Care should be taken not to press on the cornea. Firm pressure to the point of pain is applied for about twenty-five to thirty seconds

Eyeball pressure may cause detachment of the retina in patients who have myopia

3. Frequently, the patient is able to stop the attack himself by deep breath-holding or the Valsalva procedure (attempted forced inspiration with the glottis closed) or the Muller procedure (attempted forced expiration with the glottis closed), or by changing his posture, stooping or bending over

4 *Induction of Vomiting* —An increased vagal tone can be obtained by causing the patient to vomit Syrup of Ipecac (USP) is very effective for this purpose The initial dose is from 4 to 8 cc. orally, repeated every hour until vomiting occurs In some cases, the attack may cease a few minutes before emesis occurs Side effects, such as weakness, sweating, a drop in blood pressure, and pallor and diarrhea may occur but are not significant

B. The Use of Parasympathomimetic Drugs —Mecholyl (acetyl-beta-methylcholine), neostigmine (prostigmine) and other parasympathomimetic drugs have been used in the treatment of paroxysmal auricular tachycardia

Mecholyl —An initial dose of 5 to 15 mg. can be given subcutaneously. When effective, the attack stops in a few minutes. If the initial dose is ineffective, it can be repeated in twenty minutes Undesirable side reactions are very common It is necessary to have the patient lying to prevent syncope. In addition, marked perspiration, salivation, flushing of the face,

epigastric discomfort, nausea, vomiting or involuntary defecation, generalized convulsions or cardiac arrest may occur. A rapid antidote for mecholyl is the intravenous injection of 0.5 to 1 mg. of atropine, which should be available in a syringe before the mecholyl is injected. Because of these side reactions I have rarely used mecholyl.

Mecholyl can also be used intranasally. A vial containing 25 mg. is dissolved in just sufficient tap water to saturate a cotton pledget, which is inserted well into the nose. The pledget is removed as soon as the heart rate slows

Neostigmine —Neostigmine (prostigmine) has been used in place of mecholyl in a dose of 0.5 to 2 mg. subcutaneously, but I have found it less effective than mecholyl in stopping attacks of paroxysmal tachycardia.

C. QUINIDINE —Quinidine is an excellent drug for stopping attacks of paroxysmal tachycardia. It also can be used in cases of paroxysmal auricular fibrillation, auricular flutter and ventricular tachycardia.

Quinidine does not act through the vagus nerve but has a direct depressant effect on the heart muscle and conduction system, prolonging the refractory period of heart muscle, decreasing its excitability, and decreasing the rate of conduction of stimuli through the conduction system. Inasmuch as quinidine is rapidly absorbed through the gastrointestinal tract, it is usually given orally Recent observations have indicated that large doses of quinidine, spaced several hours apart, are more effective than smaller doses given hourly. Although some effects of quinidine persist for eight or ten hours or longer after oral administration, the maximum effect is reached in about four hours. Since the therapeutic effect of quinidine is related to the concentration it reaches in the blood (the average effective blood level is 5 mg. of quinidine per liter of blood), the drug should be given every few hours, day and night, to obtain maximum therapeutic results.

In administering quinidine, it is customary to give a test dose of 0.2 gram (3 grains) and to wait several hours before starting the regular doses in order to detect serious reactions which might appear. However, in those cases where serious reactions have occurred in my experience, the test dose was taken without difficulty.

A dose schedule that I have found effective is 0.4 gram (6 grains) every two hours, day and night, until the tachycardia stops or until toxicity appears However, I have rarely found it necessary to use more than 4 grams (60 grains) (10 doses in twenty hours) to stop an attack of auricular tachycardia. In refractory cases, or where the patient's condition is critical, as much as 0.66 gram (10 grains) can be given every two hours for twenty-four hours, making a total dose of 8 grams (120 grains). If the tachycardia persists after such massive doses of quinidine, the quinidine should be temporarily stopped. However, signs of toxicity usually develop rapidly when doses larger than 4 grams a day are used, and may force discontinuance of the drug before a therapeutic result is achieved.

When the tachycardia stops, the quinidine should be continued at half the maximum dose for the next twenty-four hours. The dose is then gradually decreased to 1.2 grams (18 grains) daily in several days, and the drug may be stopped within a week.

Another method of using quinidine sulfate orally is the following: An initial dose of 0.2 to 0.6 gram (3 to 9 grains) is given and repeated every two hours for 3 or 4 doses. If the condition remains unchanged the size of the dose is increased by 0.1 or 0 2 gram (1½ to 3 grains) This larger dose is continued every two hours for 3 or 4 doses. At this time, if the tachycardia is still present, the quinidine is continued every two hours, but the dose is increased each time by 0 1 or 0.2 gram (1½ to 3 grains) It is rarely necessary to raise the dose above 1.2 grams (18 grains) to stop the tachycardia, although in one case under my observation it was necessary to raise the dose to 2 grams to achieve a therapeutic response. Such large doses are dangerous, and an electrocardiogram should be taken before each dose in order to detect toxic electrocardiographic signs (see below).

Quinidine can also be given intramuscularly and in desperate cases intravenously Preparations available for intramuscular use include quinidine dihydrochloride, quinidine hydrochloride (with 15 per cent antipyrine and urea added to keep the quinidine in solution), and quinidine lactate The average intramuscular dose is 0 5 gram (7½ grains) The quinidine begins to act within fifteen to thirty minutes after intramuscular injection, reaching a maximum effect in one and a half to three hours The dose can be repeated every two hours if necessary

If used intravenously, these preparations are best administered by adding the contents of an ampoule to 50 cc of a 5 per cent glucose solution, and allowing the contents to run into the vein at a rate of 2 cc per minute The patient should be connected to a direct-writing electrocardiograph, and the infusion stopped when the tachycardia stops or if signs of toxicity appear If the tachycardia is still present when the entire solution has run in, and if no signs of toxicity are present, another ampoule can be similarly dissolved and used. This procedure can again be repeated as necessary

Quinidine sulfate can also be prepared for intravenous use in an 0.8 per cent solution (it is poorly soluble in water) Four grams are dissolved in 500 cc saline or 5 per cent glucose in distilled water, by shaking vigorously. It is given intravenously at a rate of 10 to 40 drops a minute until the tachycardia stops or toxicity develops

Toxicity.—Regardless of the route by which the quinidine is given, or the salt of quinidine used, toxic manifestations occur very frequently. Some of the more common toxic symptoms are tinnitus, nausea, vomiting, diarrhea, headache or dizziness These have been described as cinchonism. However, the drug need not be discontinued unless these symptoms become distressing to the patient. Often, if the quinidine is stopped and then readministered more slowly, the patient will be able to tolerate even larger doses than those which caused symptoms previously. However, there is no direct relation between plasma quinidine levels and the development of toxicity. *Paregoric* can be used to control the gastric irritation and diarrhea produced by quinidine.

More serious symptoms are blurring of vision, scotomata, photophobia or diplopia, disturbances of color perception, macular, papular, or urticarial or exfoliative skin rashes or thrombocytopenic purpura, fever, difficulty of breathing, collapse, mental confusion or convulsions, or respiratory arrest.

Toxic cardiac manifestations are also common These include incomplete or complete *a–v* block, sinus arrest, auricular standstill, prolongation of the *QRS* interval to 0 12 second or the development of bundle branch block if the *QRS* has previously been normal, or prolongation of the *QRS* more than 25 per cent if bundle branch block had been present, ventricular premature contractions, ventricular tachycardia or ventricular fibrillation. The development of a prolongation of the *P–R* interval, or prolongation of the *Q–T* interval or lowering or reversal of the *T* waves or *RS–T* deviations should not be considered as indications for discontinuing the drug. However, when one of the other electrocardiographic abnormalities appears, the drug should be stopped, because death may occur suddenly. This is the reason that daily electrocardiograms should be taken on patients receiving 4 grams (60 grains) or more of quinidine daily; and when repeated single doses of more than 0 6 gram (9 grains) are given, an electrocardiogram should be taken before each additional dose.

Contraindications —Quinidine should not be used if there is a history of serious reactions to it In addition, it should not be prescribed to patients with complete *a–v* block, because it can precipitate ventricular fibrillation or cardiac standstill (also see page 330)

Antidotes. —There is no specific antidote for quinidine. If respiratory depression or arrest occurs, caffeine can be used. If circulatory collapse occurs, desoxyn (page 284) or other pressor agents can be used

The Simultaneous Use of Quinidine and Digitalis —Quinidine alone will often stop the tachycardia If quinidine is ineffective, it can be discontinued and the patient can be digitalized (or other measures used). However, in refractory cases, or if heart failure is present or develops, the patient can be digitalized while the quinidine is continued. There is no evidence that the simultaneous use of quinidine and digitalis is harmful, although some cardiologists have been fearful of using both drugs simultaneously As a matter of fact, better results are sometimes obtained if quinidine is given after the patient has been fully digitalized

D DIGITALIS.—An attack of paroxysmal auricular tachycardia can often be quickly stopped by digitalizing the patient rapidly. I generally use for this purpose 4 cc of lanatoside C (cedilanid) intravenously. If the tachycardia is still present after one-half hour, I try carotid sinus pressure, which is often effective after digitalization even if it were unsuccessful before, because digitalis sensitizes the carotid sinus. However, if carotid sinus stimulation is still ineffective, I give another intravenous injection of 4 cc. of lanatoside C. If the tachycardia is still present a half-hour later, I prescribe quinidine (see above).

E. OTHER DRUGS.—Many other drugs have been used to stop attacks of auricular tachycardia Some of the more successful are:

Magnesium Sulfate.—Magnesium is valuable because it has a tendency to depress the heart muscle and the conduction system. The usual dose is 10 to 20 cc of a 20 per cent solution, intravenously. This can be prepared by diluting the contents of two ampoules of 2 cc. magnesium sulfate (50 per cent) with 6 cc. of distilled water. The tachycardia should stop almost immediately after the injection. Side reactions, such as a generalized sensation of heat, perspiration, weakness, dizziness and nausea, may appear. In addition, a short run of ventricular premature contractions may develop.

Neosynephrine.—Neosynephrine and other pressor drugs have also been used in the treatment of paroxysmal tachycardia. Such drugs probably work by producing a sudden increase in blood pressure (to 160 mm or more) which stimulates the vagal fibers in the carotid sinus and aortic arch, thus stopping the tachycardia An initial dose of neosynephrine is 0 5 mg. (0 05 cc) diluted in 10 cc. of saline. Its effect occurs within a few seconds after intravenous injection The drug can be repeated in a dose of 1 mg. if the tachycardia is still present after fifteen minutes, at which time the blood pressure should have returned to the preinjection level. Side reactions, such as tingling or coolness of the skin due to cutaneous vasoconstriction and piloerection, and a sense of fullness in the head may also appear More serious is the development of a short run of ventricular premature contractions

Methoxamine hydrochloride (vasoxyl) is another pressor amine which can stop an attack of paroxysmal supraventricular tachycardia almost immediately It is particularly useful if the patient is in shock, because it has strong pressor effects also. It can be given intravenously in a dose of 5 to 10 mg, or intramuscularly in a dose of 15 mg

It is supplied in 1 cc. ampoules, each containing 20 mg

Procaine Amide—Procaine amide (page 353) may be of value in protracted cases

Prophylaxis—There is no effective way of preventing the attacks of paroxysmal tachycardia. Sedatives may be helpful The prophylactic administration of quinidine has been recommended, but daily doses of 2 grams (30 grains) or more are often necessary, and I have seen attacks occur even when the patient was on maintenance quinidine therapy. Sometimes, digitalization followed by a maintenance dose of digitalis is effective. Potassium salts may also be helpful prophylactically Any of the potassium salts can be used (page 717) in a daily dose of 1 or 2 grams (15 to 30 grains) I have often prescribed a saturated solution of potassium iodide, 10 drops 3 times daily, for this purpose, to patients with hypertensive heart disease who suffer from attacks of paroxysmal tachycardia

Summary.—The physician, confronted with the wide choice of measures which can be used to treat paroxysmal auricular tachycardia, may be somewhat confused rather than enlightened Actually, most cases will respond to either quinidine or digitalis or both. The procedures that I usually use are the following:

If I am called to see a patient for the first time, I take an electrocardiogram to confirm the diagnosis. The first procedure that I use is carotid sinus pressure, or eyeball pressure If this is not successful, I have the patient try the Valsalva procedure If the tachycardia persists, I give an intravenous injection of 4 cc of lanatoside C (cedilanid). My reason for using digitalis in preference to quinidine is that I prefer to remain with the patient until the tachycardia ceases, and I have found that this occurs more quickly with digitalis than with quinidine. If after a half-hour the tachycardia is still present, I try carotid sinus pressure and other forms of vagal stimulation again, and then give another 4 cc. of lanatoside C intravenously if the tachycardia persists. At the end of an hour, if the tachy-

cardia is still present, I prescribe quinidine, 0.4 gram (6 grains) every two hours, day and night, until the tachycardia stops, or toxicity appears

For patients who have multiple attacks, I prescribe syrup of ipecac, or quinidine, which the patient uses himself when an attack occurs. I rarely find it necessary to use the other procedures described above.

Nodal Tachycardia.—The etiology, clinical picture, course and prognosis, and treatment of nodal tachycardia are essentially the same as for auricular tachycardia It is very difficult to differentiate nodal tachycardia from auricular tachycardia even with the electrocardiogram, unless nodal *P* waves are clearly visible. On physical examination, nodal tachycardia is characterized by the production of large systolic pulsations in the neck veins, due to the more or less simultaneous contraction of auricles and ventricles. However, a similar situation may occur in auricular tachycardia (page 343)

Paroxysmal Tachycardia in Infants.—Paroxysmal tachycardia in the newborn or in infants less than one year old is not rare The ventricular rate is usually very high and may reach or exceed 300 per minute. In most cases, the attacks are due to auricular flutter with a 1 1 ventricular response (page 361) However, auricular or nodal tachycardia is also common, but paroxysmal auricular fibrillation is rare.

Etiology—The attack may follow an acute infection, but often there is no apparent etiology

Symptoms and Signs.—The ventricular rate is usually between 200 and 300 The respiratory rate may reach or exceed 50 per minute, and cyanosis may develop. Left- or right-sided heart failure may develop and the liver may descend to the pelvic brim. A rise in temperature may also occur

Diagnosis—A paroxysmal tachycardia should not be confused with a sinus tachycardia, because even in a normal newborn infant, the ventricular rate may be 150 However, in sinus tachycardia, the heart rate does not exceed 200

Course and Prognosis.—Paroxysmal tachycardia in infants is serious, and death from heart failure may occur unless the tachycardia is stopped

Treatment.—When the infant shows respiratory distress, he should be placed in an oxygen tent If an infectious process is present, antibiotics should be used

Digitalis is usually effective for the tachycardia, regardless of the type. The dose schedule described on page 263 can be used. However, infants with paroxysmal tachycardia often require massive doses of digitalis

If digitalis products are not effective, quinidine can be prescribed in a dose of 30 to 50 mg ($\frac{1}{2}$ to $\frac{3}{4}$ grain) orally every four hours. Mecholyl has also been used in a dose of 0 5 mg. intramuscularly but even with this small dose it may be necessary to give 0.05 mg. of atropine or more because of the sudden appearance of asthmatoid wheezing and bradycardia (see page 345).

Paroxysmal Tachycardia in Children—Paroxysmal tachycardia in children is treated as in adults with carotid sinus pressure and other forms of vagal stimulation, and with digitalis, quinidine and the other drugs described on pages 345 to 349 Doses of digitalis and quinidine should be approximately half the adult doses

VENTRICULAR TACHYCARDIA

Electrocardiogram (Fig. 72) —Ventricular tachycardia is produced by a succession of ventricular premature contractions which may arise from a single focus or from varying foci It shows the following characteristics:

1. The heart rate is rapid The rate is usually above 140 per minute, but may vary from 100 to 300. The rhythm may be regular or irregular.

2 The *QRS* complexes are 0.12 second wide or more, and aberrant, and are followed by aberrant *RS–T* segments and *T* waves. Frequently it is

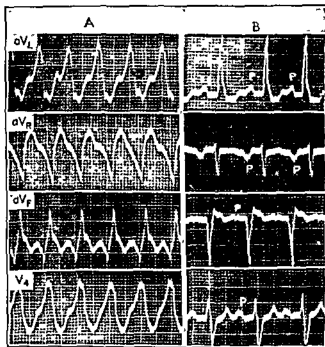


Fig 72 —Ventricular tachycardia *A*, Shows a ventricular tachycardia *B*, Taken the next day, shows sinus rhythm The Q_{aVF} is due to posterior infarction. (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed, 1953)

difficult to separate the *QRS* from the *RS–T* and *T*, and the tracing gives *the appearance of a series of large, wide, regular undulations* (Fig. 72). The term bidirectional ventricular tachycardia (Fig 73) is used when the alternate *QRS* complexes in any one lead point in opposite directions

3 *P* waves may or may not be seen. The auricles beat independently of the ventricles, usually at a slower rate, and isolated *P* waves may appear, scattered throughout the tracing. Ventricular tachycardia may also occur in a patient whose basic rhythm is complete *a–v* block, auricular flutter or fibrillation

Etiology.—While ventricular tachycardia may occur in persons who have no heart disease, it most commonly occurs in patients with coronary artery

disease It can also be produced by digitalis, quinidine and other drugs. Bidirectional ventricular tachycardia is almost always due to digitalis toxicity. Ventricular tachycardia is most frequently seen in middle-aged persons but it also occurs in young adults and adolescents

Symptoms and Signs.—The clinical picture is similar to that of auricular tachycardia (page 343) Since the auricles usually beat at a slower rate than the ventricles, the first heart sound may vary from beat to beat, due to the changing relations between auricular and ventricular systole. The situation is somewhat similar to the lack of relation between auricular and ventricular systole that occurs in complete *a–v* block Neck vein pulsations also vary in amplitude for the same reason. An unusual auscultatory phenomenon, namely, the appearance of only one heart sound, may occur. This may be confusing and may simulate a heart rate one-half of the rate which is present, especially if the patient is in shock and pulseless.

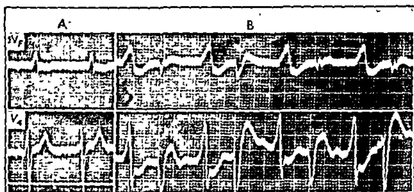


Fig 73 —Bidirectional ventricular tachycardia *A*, Shows auricular fibrillation Digitalis caused the depressed $RS\text{-}T_{aVF}$ *B*, Was taken three days later Notice the widening of the *QRS* interval and the alternate directions of the *QRS* complexes (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed, 1953)

Diagnosis.—Diagnosis is made from the electrocardiogram The differentiation of ventricular tachycardia from auricular tachycardia with bundle branch block or the Wolff-Parkinson-White syndrome is discussed on page 344

Course and Prognosis.—An attack of ventricular tachycardia may last a few seconds or minutes and spontaneously subside. However, severe attacks can last hours, days, weeks, and even months. Heart failure does not usually develop, unless organic heart disease is present. Death may occur from either heart failure or shock. Abnormal *T* waves may appear after the tachycardia stops, just as after auricular tachycardia (page 345).

Ventricular tachycardia is usually more serious than auricular tachycardia because of the underlying heart disease usually present However, when it occurs in a person who does not have heart disease, the prognosis is excellent

Treatment.—Quinidine is the drug of choice. The dosage is the same as for auricular tachycardia, page 346. In cases of ventricular tachycardia,

when quinidine is ineffective, the intramuscular or intravenous injection of 1 to 2 mg. ($\frac{1}{60}$ to $\frac{1}{30}$ grain) of atropine may restore sinus rhythm The best effects from atropine are obtained when it is injected at a time when the quinidine has succeeded in slowing the ventricular rate somewhat, even though the ventricular tachycardia is not abolished When ventricular tachycardia is due to digitalis, the digitalis should be stopped This may be sufficient to abolish the ventricular tachycardia, if only short runs are present. In other cases, potassium can be used (page 717). Quinidine has also been found helpful in such cases, but I prefer not to use it if digitalis is the cause of the tachycardia

When quinidine is used in ventricular tachycardia, electrocardiograms should be taken several times a day because the ventricular rate may slow greatly without the ventricular tachycardia being abolished. In addition, the quinidine prolongs the width of the already wide *QRS* complex. This itself is not an indication for the withdrawal of the quinidine, unless the widening of the *QRS* interval exceeds 25 per cent.

Digitalis will not stop an attack of ventricular tachycardia, but it has been used apparently successfully in some cases of ventricular tachycardia in conjunction with quinidine, where quinidine alone was unable to restore sinus rhythm. It should also be used if the patient with ventricular tachycardia develops heart failure, except in those cases where the ventricular tachycardia is due to digitalis.

Other drugs that have been used with some success in ventricular tachycardia include magnesium sulfate (page 348), and morphine intravenously in a dose of 15 to 30 mg. ($\frac{1}{4}$ to $\frac{1}{2}$ grain).

Procaine amide hydrochloride (*pronestyl hydrochloride*) has recently been used successfully in ventricular tachycardia, ventricular premature beats and even in paroxysmal auricular tachycardia, auricular fibrillation or auricular flutter The drug has a direct depressant effect on the ventricular muscle and may be effective in cases which do not respond to quinidine. It has less effect on the auricles It can be given orally or intramuscularly Intravenous injection should be used only for emergencies.

The following dose schedule can be used:

Ventricular Tachycardia.—One gram (4 capsules) orally, followed by 0 5 to 1 gram (2 to 4 capsules) every four to six hours as indicated

Intramuscularly, the initial dose is 1000 mg. (10 cc), given undiluted. The injection does not cause pain. An effect may be noted within three to fifteen minutes Peak effects occur within an hour. An effect may last from two to ten hours after a single injection Subsequent doses of 200 to 1000 mg (2 to 10 cc) may be given at intervals of one to six hours, depending on the severity of the condition and response of the arrhythmia.

Intravenously, the drug should be given at a rate which does *not* exceed 100 mg (1 cc.) per minute, and no more than 1 gram should be given in one dose. Hypotension or shock may occur Electrocardiographic tracings should be made during the injection and the injection stopped when the tachycardia disappears, or if the *P–R* interval or the *QRS* widens (see below).

Ventricular Premature Beats—Two capsules (0 5 gram) can be given every four to six hours orally, as indicated.

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If liver and kidney disease are present, accumulation of the drug can occur and continued administration can be dangerous.

Auricular Arrhythmias.—The total daily oral dose ranges from 1 to 5 grams, given in three or four divided doses. Initially, 1.25 grams (5 capsules) can be given. This can be followed by 0.75 gram (3 capsules) in two hours if there are no electrocardiographic changes. Several further doses of 0.5 to 1 gram (2 to 4 capsules) can be given every two hours, until the auricular tachycardia stops. At this time, a maintenance dose of 0.5 to 1 gram (2 to 4 capsules) every three to six hours can be used.

Intramuscularly, and intravenously, 500 mg. to 1 gram (5 to 10 cc.) can be given. The intravenous dose must be given at a rate which does *not* exceed 100 mg. (1 cc.) per minute.

During the course of anesthesia, procaine amide can be given intravenously in a dose of 100 to 500 mg. (1 to 5 cc.), at a rate which does not exceed 200 mg. (2 cc.) per minute. During anesthesia, the danger of hypotension or shock from intravenous procaine amide is much less than in conscious patients.

In cases where quinidine had been used and one wishes to change to procaine amide, one should remember that procaine amide is about one-fourth to one-third as strong as quinidine by weight. Therefore, one can be substituted for the other according to the rule that 0.25 gram (1 capsule) of procaine amide is equivalent to 0.065 gram (1 grain) of quinidine.

Toxicity of Procaine Amide.—The action and toxicity of procaine amide are very similar to those of quinidine. Transient electrocardiographic changes, including a lowering of the amplitude of *T*, slight prolongation of the *P–R* interval and slight prolongation of the *QRS* interval and the *Q–T* interval, may occur. These changes usually disappear within thirty minutes after intravenous injection of the drug. They rarely appear after oral administration.

More serious toxic manifestations include widening of the *P–R* interval beyond 0.2 second, or widening of the *QRS* interval more than 25 per cent of its original width. In addition, ventricular premature beats, ventricular tachycardia and cardiac arrest may occur from procaine amide.

Procaine amide may also cause side effects such as nausea, vomiting, diarrhea, dizziness, headache, mental confusion, pruritis, chills and fever. Respiratory depression, or marked hyperpnea may occur, and even convulsions. Agranulocytosis may also occur when the drug is used over long periods of time. This can be prevented by doing a white blood count every month.

Although preliminary reports on the efficacy of procaine amide in ventricular tachycardia have been enthusiastic, I have observed several cases where it was not effective.

Prophylaxis.—There is no completely effective prophylactic therapy, although quinidine and pronestyl can be used. (See also Prophylaxis of Auricular Tachycardia, page 349.)

VENTRICULAR FIBRILLATION

In ventricular fibrillation, the normal effective ventricular contractions are replaced by rapid, incoordinate, ventricular undulations so that

the heart stops beating effectively, and syncope, convulsive movements and death will occur within a minute or so unless the ventricular fibrillation is arrested

Electrocardiogram (Fig 74) —The electrocardiogram shows large, wide, continuous waves that are irregular in size, shape, width and rate. *P* waves are not seen, although the auricles can continue to beat during ventricular fibrillation.

Etiology.—Ventricular fibrillation can occur in the following ways:

1 As a terminal event in moribund patients The heart may continue to show ventricular fibrillation for half an hour or more after clinical death.

2 Due to electric shock or anesthesia It has even resulted from carotid sinus pressure

3 As a result of digitalis or quinidine toxicity

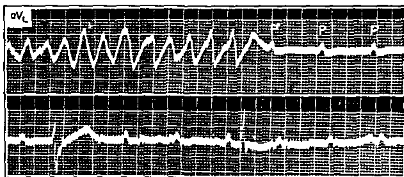


Fig 74 —Transient ventricular fibrillation in a patient with complete *a–v* block The upper and lower rows are a continuous strip (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed, 1953)

4. Transient ventricular fibrillation may occur in patients with complete *a–v* block, producing the Adams-Stokes syndrome (page 328). Such attacks are often preceded by runs of ventricular premature contractions Transient ventricular fibrillation of this type can be precipitated by small therapeutic doses of quinidine or digitalis

5 Transient ventricular fibrillation may also occur spontaneously in *persons who have no apparent signs of heart disease*

Course and Prognosis.—Ventricular fibrillation usually indicates that death is at hand However, patients with complete *a–v* block may have attacks of transient ventricular fibrillation for many years, and a heart which has developed ventricular fibrillation can be restored to sinus rhythm, if the heart can be exposed, as during surgical procedures

Treatment —The treatment of ventricular fibrillation developing during surgical operations is described on page 763. There is at present no effective treatment for ventricular fibrillation due to other conditions The intracardiac injection of epinephrine has been described as successful, but this is questionable (see page 330)

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Chapter 20

AURICULAR FLUTTER AND AURICULAR FIBRILLATION

AURICULAR FLUTTER

In auricular flutter, the auricles beat at a rapid rate varying from 200 to 380 per minute, and in auricular fibrillation, the auricular rate is from 380 to 600 or more. It has been generally taught that auricular flutter is produced by the continuous spread of a stimulus through the auricles in a very constant and regular circular path around the orifices of the superior and inferior vena cavæ (circus movement), whereas in auricular fibrillation, the increased rate of the spread of the stimulus (and other factors) causes its path to become more irregular. This concept has been challenged recently, and there is evidence that in many cases auricular flutter is similar to paroxysmal auricular tachycardia and that the stimulus spreads outwardly through the auricles from a single ectopic focus in a radial direction, just as a normal stimulus does, and that there is no circus movement.

Regardless of which theory is correct, auricular flutter and fibrillation can be considered as variants of the same phenomenon, namely, the rapid formation of ectopic auricular stimuli, a major difference between the two arrhythmias being that in auricular flutter the stimulus spreads through the auricles at a slower rate and through a more regular path than in auricular fibrillation Thus, when auricular flutter is present, and the auricular rate exceeds 380 or 400, auricular fibrillation appears. When auricular fibrillation is present and the auricular rate slows to less than 400, auricular flutter appears

Etiology.—Auricular flutter may occur in normal people It may appear in hyperthyroidism, acute myocardial infarction, during acute pulmonary infections, and is common in rheumatic heart disease, especially mitral stenosis Paroxysmal auricular flutter with a 1:1 ventricular response is common in infants Rarely, auricular flutter is produced by digitalis toxicity Occasionally, it occurs in association with auricular tachycardia

Symptoms.—The symptoms of auricular flutter depend on the ventricular rate. In cases of paroxysmal auricular flutter where the ventricular rate may be very rapid, even 300 or more, the clinical picture is that of auricular tachycardia (see page 341) However, when the ventricular rate is low, the patient may be unaware of the arrhythmia.

Signs.—Since the auricular rate in the average case of auricular flutter is between 200 and 360, and some degree of *a–v* block is usually present, the ventricular rate is usually between 70 and 160 (Also see page 364) However, as I pointed out above, the ventricular rate may rise to 300 or more.

Examination of the neck veins often reveals small, rapid pulsations at a rate above 200, produced by the auricular flutter. These neck vein pulsa-

tions are not always visible. They can sometimes be accentuated by pressing gently on the jugular vein while the patient is lying flat in bed. These small venous pulsations appear during the intervals between the radial pulse beats. In addition, large neck vein pulsations may appear, synchronous with the radial pulse, due to simultaneous auricular and ventricular systole.

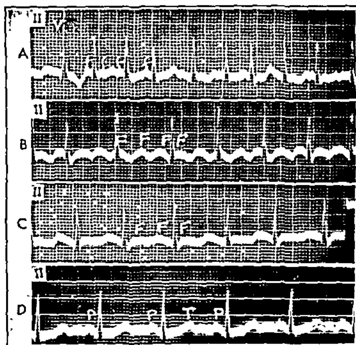


FIG. 75.—The effect of quinidine on auricular fibrillation in a woman with mitral stenosis.

A, Shows auricular fibrillation. The ventricular rate is rapid, and a ventricular premature contraction, V, is also present. The patient had been taking digitalis.

B, 0.4 gram (6 grains) of quinidine had been given an hour previously. Auricular flutter, *F*, is now present. The ventricles are beating more slowly but irregularly at a rate of approximately 100 a minute.

C, An hour later, after 0.2 gram (3 grains) more of quinidine had been given. Auricular flutter is still present. The ventricles are still beating irregularly at a rate of approximately 100 a minute.

D, Quinidine was continued, 0.2 gram (3 grains) every hour for four more doses, when the heart rate became completely regular.

D, Taken the next morning, shows sinus rhythm. (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed., 1953.)

Auscultation of the heart may reveal faint sounds due to the auricular flutter, in addition to the two heart sounds, which may have a tic-toc, embryocardia rhythm. When the ventricular rate is irregular, the character of the first heart sound may change markedly from beat to beat due to the changing relations between auricular and ventricular systole, just as occurs in cases of ordinary *a–v* block (page 158). Examination of the heart may also reveal signs of underlying organic heart disease.

Fluoroscopic examination may show two or more auricular contractions to each ventricular contraction.

Electrocardiogram.—The auricular flutter or *F* waves are characterized by the following:

1 One complete flutter cycle consists of an upward wave followed by a downward wave (Fig. 75, *B*). The upward and downward peaks of the flutter wave may be sharp, rounded, or notched In precordial leads $V_{1,2}$ and in esophageal leads, the *F* waves may resemble large biphasic *P* waves. Some leads show the *F* waves better than others, depending on the direction in which the stimulus spreads through the auricles. Lead I usually shows the *F* waves very poorly

2 A continuous sequence of *F* waves occurs, and in the augmented unipolar extremity and standard leads, a saw-tooth effect is often produced. The *F* waves become distorted where they are superimposed on the *QRS* complex, *RS–T* segment and *T* wave.

3 The rate at which the auricles flutter varies from about 200 to 380 per minute, with an average rate of 300. Quinidine may slow the flutter rate to below 200 The flutter rate in any one case is very constant even over long periods of time. The flutter rate is measured from the interval between any two successive *F* waves (see page 84).

4. Although the *a–v* node can at times respond to stimuli as rapid as 300 per minute, some degree of *a–v* block is usually present Thus, if the auricles are fluttering at a rate of 300 and every other stimulus that reaches the *a–v* node is blocked, the ventricles beat at a regular rate of 150 per minute This can be called auricular flutter with a 2:1 *a–v* block, because there are two flutter waves for each *QRS* complex 4:1, 5:1, or even complete *a–v* block can occur Occasionally, 1:1 flutter occurs.

5 Although it is not possible to describe a *P–R* interval in cases of auricular flutter, the *QRS* complexes usually have a fixed relation to the peaks of the flutter waves throughout the tracing, and the ventricular rate is usually regular. Occasionally the ventricles do not respond so regularly to the flutter waves, and slight irregularity of the ventricular rhythm occurs When the ventricular rate is rapid, it may be impossible to recognize the *F* waves, and the tracing must merely be diagnosed as "supraventricular tachycardia" (page 341)

6 Vagal stimulation by means of carotid sinus pressure, *etc.*, tends to aggravate the degree of *a–v* block and transient slowing of the ventricles occurs, but the flutter rate usually remains unchanged Rarely, the rate increases and a short run of auricular fibrillation may appear. Exercise *may increase the ventricular rate but does not change the flutter rate*

Diagnosis —When auricular flutter is present and the ventricular rate is rapid, it can simulate paroxysmal auricular or nodal tachycardia, ventricular tachycardia or paroxysmal auricular fibrillation. Carotid sinus pressure is often helpful in establishing the diagnosis clinically. If auricular flutter is present, carotid sinus pressure often, but not always, causes the ventricular rate to slow markedly, and when the pressure is discontinued, the ventricular rate increases in an irregular manner to its previous level. This is in contrast to the effect of carotid sinus pressure on auricular or nodal tachycardia, where it may cause a prompt decrease in the ventricular

rate, which remains low, even when the pressure is discontinued. However, carotid sinus pressure may cause a response in cases of auricular or nodal tachycardia, similar to the response in auricular flutter. Carotid sinus pressure has no effect on ventricular tachycardia or auricular fibrillation.

The ventricular rate itself may be used as a means of differential diagnosis Since in most cases of auricular flutter the auricular rate varies from 200 to 360, and since there is usually some degree of *a–v* block present, the ventricular rate is usually 160 or less. Thus, if auricular flutter were present *with a rapid regular ventricular rate of 200, it would mean that the* auricles are fluttering at a rate of 200 and a 1·1 *a–v* block is present, which is extremely rare (I have seen it only once), or it would indicate that the auricles are fluttering at a rate of 400 with a 2 1 *a–v* block, but flutter rates so high are also rare. Thus a ventricular rate in the range of 200 itself suggests that auricular flutter is not present.

When auricular flutter with a slow ventricular rate is present, it can simulate sinus rhythm or auricular fibrillation. The presence of small rapid neck vein pulsations which are present during the diastolic pauses of the radial pulse itself rules out sinus rhythm However, one should not mistake the normal triple undulations of the *a*, *c*, and *v* venous waves that occur with each normal heart beat for auricular flutter. Another point of differentiation is that if auricular flutter is present, auscultation of the heart may reveal extra heart sounds, which are not present in sinus rhythms.

Exercising the patient may also help differentiate auricular flutter from sinus rhythms In auricular flutter, the ventricular rate may suddenly rise to double its previous level after moderate exercise, such as knee-bending or hopping, when the degree of *a–v* block lessens. For example, if the auricles are fluttering at a rate of 300, and a 4·1 *a–v* block is present, the ventricular rate is 75 If exercise converts the *a–v* block to a 2:1 block, the ventricular rate suddenly rises to 150, and then slowly and irregularly returns to its previous level. If sinus rhythm is present, there would be a gradual and not so marked increase in heart rate to 98, 112 or some other odd figure, followed by a slow and gradual return to its former level.

Auricular flutter can often be differentiated from auricular fibrillation in the following ways: after exercise, the ventricular rate in auricular flutter not only may increase to double its former level, but it becomes regular for a short time, whereas, exercise increases the ventricular rate in auricular fibrillation but it remains or becomes markedly irregular. Auscultation of the heart may also be helpful in differentiation because if the ventricular rate in auricular flutter is irregular, much more marked variations in the intensity of the first heart sound are present than in auricular fibrillation, because in flutter, the variations in the intensity of the first heart sound are due to the changing relations between auricular and ventricular systole, whereas in auricular fibrillation, the auricles remain functionally in diastole, *and the variations in the intensity of the first heart sound are* related to the length of the diastolic pause and the filling of the ventricles.

Course and Prognosis.—Auricular flutter may be paroxysmal or permanent, and cases have been reported where it persisted for twenty or more years. In most cases, it can be converted to either auricular fibrillation or

sinus rhythm. However, it may prove refractory to treatment. So long as the ventricular rate is slow, it is not serious However, when it occurs with a rapid ventricular rate in patients with acute myocardial infarction or organic heart disease, fatal heart failure or shock may occur unless the ventricular rate is slowed

Treatment.—Auricular flutter should be converted to sinus rhythm if possible. Quinidine or digitalis can be used Procaine amide is also effective in paroxysmal flutter.

Digitalis.—Digitalis increases the rate at which the auricles flutter, and thus converts auricular flutter into auricular fibrillation When this occurs and the digitalis is stopped, the auricular fibrillation usually spontaneously disappears and normal sinus rhythm reappears This may take one or two days or a week or longer. However, if auricular fibrillation is still present a week after the digitalis has been stopped, a spontaneous change to sinus rhythm will probably not occur. In some cases, the auricular fibrillation may later change to sinus rhythm even if it is necessary to maintain digitalis because of the presence of heart failure The reason why sinus rhythm appears after auricular fibrillation has been produced by digitalis is not known. The chances of it happening can be increased by giving sufficient digitalis so that the auricular flutter is not only converted to fibrillation but the ventricular rate is slowed markedly Occasionally, the auricular fibrillation reverts to auricular flutter when the digitalis is discontinued

Quinidine.—Quinidine slows the rate at which the auricles flutter, and usually restores sinus rhythm Occasionally it merely produces a slow auricular flutter and a slow regular ventricular rate without restoring sinus rhythm This is the reason that an electrocardiogram should be taken after quinidine has been given for auricular flutter Quinidine usually slows the ventricular rate when auricular flutter is present This is due to a direct depressant effect on the *a–v* node, which aggravates the degree of *a–v* block

Quinidine may also increase the ventricular rate when given to a patient with auricular flutter, in the following way for example, if a patient with a flutter rate of 400 and a 4 1 *a–v* block is given quinidine, the flutter rate may fall to 300, but more of the auricular stimuli may be conducted through the *a–v* node, and a 2 1 *a–v* block may temporarily occur. The ventricular rate may therefore temporarily increase from 100 to 150 This is the reason that quinidine is often used in combination with digitalis in cases of auricular flutter, the digitalis acting to maintain a high degree of *a–v* block.

In practice, my usual procedure is to digitalize the patient with lanatoside C intravenously or intramuscularly, to convert the auricular flutter to auricular fibrillation, and in addition, try to decrease the ventricular rate to about 70 This may require more than the ordinary digitalizing doses (see page 257) The digitalis is then stopped and forty-eight hours allowed to elapse If sinus rhythm has not appeared, a maintenance dose of one of the digitalis preparations is prescribed (see page 258) and the patient is given quinidine (see page 346 for dose schedule).

AURICULAR FIBRILLATION

In auricular fibrillation, the normal auricular contractions are replaced by a continuous series of rapid, irregular, fibrillatory waves at a rate of 380

to 600 or more a minute, which are ineffective in emptying the auricles so that functionally the auricles remain in diastole.

Pathology.—Inflammatory and degenerative changes with fibrous replacement are common in the auricles in cases or auricular fibrillation, but such changes may occur in the absence of fibrillation. There is therefore no specific lesion in the auricles responsible for, or pathognomonic of auricular fibrillation

Etiology.—Auricular fibrillation may occur in otherwise normal adults. However, it is also common in hypertensive cardiovascular disease, in rheumatic heart disease, especially with mitral stenosis, and in hyperthyroidism where it may be either paroxysmal or permanent. It has also been produced experimentally in man by giving acetyl-b-methylcholine to patients with hyperthyroidism. It can occur as a result of digitalis toxicity, after trauma to the heart, or trauma to the head, and has been reported even after severe physical exertion or emotional upsets. It is more common in adults than in children and is rare in infants. In children it may occur during the course of acute rheumatic fever It has also been reported as a familial disturbance

Symptoms.—Symptoms depend on the ventricular rate When paroxysmal auricular fibrillation occurs with a rapid ventricular rate, the clinical picture is that of paroxysmal auricular tachycardia (page 343), and collapse or even heart failure may develop. When the ventricular rate is slow, the patient is often unaware of the arrhythmia.

Signs.—There is usually complete irregularity of the rate, rhythm, and force of the heart beat which is easily demonstrable by palpating the radial artery. When the ventricular rate is rapid, many of the ventricular beats may be so weak that the aortic valves do not always open and blood is not expelled, so that the heart rate at the radial artery will be much slower than at the apex (pulse deficit) A pulse deficit can also occur if the force of expulsion of blood is so weak that when the pulse wave reaches the radial artery it is too feeble to be palpable. This is the reason that in cases of auricular fibrillation the ventricular rate should always be determined at the apex, by auscultation. The neck veins show an irregular pulsation, synchronous with the radial pulse (see page 151)

The Heart.—Both the first and second heart sounds vary in intensity from beat to beat, variations in the intensity of the sounds depending on the length of the preceding diastolic pause and on other factors In addition, when a ventricular contraction is too weak to open the semilunar valves, the second sound will be absent Auricular fibrillation does not produce murmurs, and when the ventricles are beating rapidly, it may be difficult to hear the murmurs of associated heart disease. In addition, the presystolic murmur of mitral stenosis disappears when auricular fibrillation develops, due to the absence of effective auricular contraction

Electrocardiogram.—The auricular fibrillation or *f* waves show the following characteristics:

1. They appear as fine, irregular undulations in the tracing (Fig. 75, *A*). In precordial leads near the sternum, and in esophageal leads, large biphasic fibrillation waves may appear. The *f* waves are continuous, and when they are superimposed on the *RS–T* segments and *T* waves, they often greatly

distort the shape of *RS–T*. The fibrillation rate can be measured from the interval between the peaks of two successive *f* waves

2 Marked irregularity in the size and shape of the *f* waves occurs from moment to moment. This is due to the irregular path of the stimulus through the auricles.

3 When the auricles are fibrillating at a relatively slow rate, the *f* waves tend to resemble the *F* waves of auricular flutter When this happens, the tracing is often called coarse auricular fibrillation, impure auricular flutter, or flutter-fibrillation

4. The ventricular rate is usually totally irregular for several reasons: Many of the auricular stimuli are blocked at the *a–v* node or are too weak to penetrate it, digitalis, which is often prescribed also increases the degree of *a–v* block, and ventricular premature contractions may also be present.

When the ventricular rate is rapid, it may be difficult to recognize the *f* waves. In such a case, the tracing can be described as a "supraventricular tachycardia" (page 341)

Diagnosis.—When the ventricular rate is rapid, auricular fibrillation may simulate auricular, nodal, or ventricular tachycardia or auricular flutter The differentiation of these conditions is described on page 363 The differentiation of auricular fibrillation from premature contractions is described on page 141 In patients with auricular fibrillation who have been given digitalis, the ventricular rate may decrease to 60 or less and become very regular as a result of complete *a–v* block. The differentiation between this and nodal rhythm or sinus bradycardia is described on page 150

Course and Prognosis—Auricular fibrillation may be paroxysmal, transient or permanent When the ventricular rate is rapid, auricular fibrillation may precipitate heart failure even if the heart is otherwise normal. However, patients with auricular fibrillation and a slow ventricular rate may live for twenty or more years in comfort. Auricular fibrillation, if untreated, does not usually spontaneously revert to sinus rhythm, although cases have been reported in which this occurred even after the auricular fibrillation had persisted for years.

Auricular fibrillation may lead to the following complications:

1. *Heart Failure.*—I mentioned above that heart failure may develop in a previously normal person as a result of paroxysmal auricular fibrillation with a rapid ventricular rate However, in patients with organic heart disease, the occurrence of auricular fibrillation, even with a comparatively slow ventricular rate, may so lower the cardiac output that heart failure occurs or persists in spite of treatment.

The reason that auricular fibrillation can lead to heart failure even in a previously normal person whereas ordinary attacks of paroxysmal tachycardia do not cause heart failure in the absence of organic heart disease is that in auricular fibrillation the auricles no longer contract, thus decreasing cardiac filling. This is aggravated by the rapid, irregular ventricular rate which also results in poor ventricular filling and a marked decrease in cardiac output.

2. *Auricular Thrombosis and Embolism*—Stagnation of blood occurs in the auricular appendages as a result of the ineffective auricular contractions and thrombus formation is common in either the right or left auricle

or both. Another factor which may be responsible for thrombus formation is the presence of inflammatory changes in the auricular endocardium. Small fragments of these thrombi may break off and embolize from the left auricle to the systemic circulation, and from the right auricle to the lungs, so that cerebral, renal, splenic, or peripheral, *etc.*, embolism, or pulmonary embolism and even death may occur.

These emboli may first appear shortly after the auricular fibrillation has been converted to sinus rhythm, small fragments of the auricular thrombus presumably being broken off by the forceful, normal, auricular contractions This is one of the reasons that attempts to convert chronic auricular fibrillation to sinus rhythm have been discouraged. However, emboli from the auricular thrombi often occur while the patient is fibrillating, and there is evidence that further embolism can be prevented in such cases by restoring sinus rhythm

Treatment.—Auricular fibrillation can be treated in one of two ways:

A Conversion of Auricular Fibrillation to Sinus Rhythm.—In cases of paroxysmal auricular fibrillation, or in cases where the auricular fibrillation seems to be an important factor in causing or maintaining heart failure, or in cases where multiple emboli are occurring from auricular thrombi, an attempt should be made to convert the auricular fibrillation to sinus rhythm Quinidine is the drug of choice. It slows the rate at which the auricles fibrillate and thus can convert auricular fibrillation into auricular flutter and then to sinus rhythm However, in many cases, there seems to be a direct transition from auricular fibrillation to sinus rhythm after quinidine. Dosage of quinidine is described on page 346 Quinidine is successful in from 50 to 90 per cent of the cases, and sinus rhythm will be maintained in about half these cases. In the other half, auricular fibrillation returns usually in a few days, or weeks.

Other drugs have also been recommended to convert auricular fibrillation to sinus rhythm Atabrine in a dose of 0.4 mg , diluted in 10 cc. of normal saline has been used intramuscularly. I have occasionally succeeded in converting paroxysmal auricular fibrillation to sinus rhythm by using a large oral dose of potassium chloride (10 grams in 20 cc. of water). Rarely, digitalis will convert auricular fibrillation to sinus rhythm, but this is unusual. The usual ineffectiveness of digitalis in converting auricular fibrillation to sinus rhythm is due to the fact that digitalis ordinarily increases the rate at which the auricles fibrillate and thus tends to perpetuate the auricular fibrillation.

Procaine amide (page 353) is occasionally successful in restoring sinus rhythm in either auricular fibrillation or flutter

When chronic auricular fibrillation is present in patients with severe heart failure and greatly enlarged hearts, or in cases of mitral stenosis or hyperthyroidism, it is usually unwise to convert such cases to sinus rhythm, not so much because of the dangers of embolization after sinus rhythm is restored, but because such patients have a tendency to revert to auricular fibrillation very quickly

It has been suggested that when a patient in chronic auricular fibrillation is to be converted to sinus rhythm, prophylactic anticoagulant therapy (page 605) *be started and maintained ten or more days before the quinidine*

is begun, in an attempt to prevent embolic complications I do not believe that this is necessary

B. Maintenance of Auricular Fibrillation.—It is not the auricular fibrillation that disturbs cardiac function but the rapid ventricular rate that so often is present. Therefore most patients with auricular fibrillation who develop heart failure can be compensated by slowing the ventricular rate with digitalis and other measures which control heart failure, even though the fibrillation persists

Digitalis causes the ventricular rate in auricular fibrillation to slow in the following ways

1. It decreases conduction through the *a–v* node, both as a vagal effect, and by directly affecting the conductivity of the *a–v* node. It may even produce complete *a–v* block in the presence of auricular fibrillation, causing the ventricular rate to fall to 60 or less.

2. Digitalis also causes cardiac slowing in an indirect way by increasing the cardiac output and improving the state of the circulation.

When auricular fibrillation develops because of hyperthyroidism or in the course of acute carditis, digitalis is often ineffective in controlling the ventricular rate, and measures directed against the underlying condition *should be used, because if large doses of digitalis are given, serious toxic* manifestations may develop

Prophylaxis.—There is no effective prophylaxis against auricular fibrillation Quinidine can be used, but it must be given in large doses When repeated attacks of paroxysmal auricular fibrillation occur, the patient should be checked for hyperthyroidism

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Chapter 21

BUNDLE BRANCH BLOCK

BUNDLE branch block exists when the passage of a stimulus through the right or left bundle of His (page 316) is interrupted. Bundle branch block is usually considered to be a pathological disturbance, and in the studies that have been made correlating the electrocardiographic patterns of right or left bundle branch block with pathological changes in the interventricular septum and the conduction system, it has been found that regardless of whether the electrocardiogram shows right or left bundle branch block, signs of injury to both bundles of His are usually present. However, right or left bundle branch block can exist as a physiological rather than pathological disturbance of conduction in many cases.

RIGHT BUNDLE BRANCH BLOCK

Pathological Physiology.—Because the stimulus cannot spread normally through the right bundle of His to the right ventricle, the stimulation of the right ventricle is delayed so that comparatively marked asynchronism between the contraction of the left and right ventricles may occur However, this does not disturb cardiac function

Etiology.—Right bundle branch block can occur in normal people, or in patients with organic heart disease In itself, it is not a sign of heart disease, and may merely represent a physiological variation of conduction. It may be transient or permanent. The electrocardiographic patterns of bundle branch block may occur in every *QRS* complex, or may appear only occasionally

Transient right bundle branch block may occur normally, and frequently after pulmonary embolism or myocardial infarction. Permanent right bundle branch block also may occur normally, but is often found in association with rheumatic heart disease, hypertensive cardiovascular disease and myocardial infarction (but here it shows electrocardiographic patterns of both the right bundle branch block and the myocardial infarction).

Symptoms.—There are no symptoms of right bundle branch block.

Signs.—Because of the asynchronous contraction of the right and left ventricles which occurs, splitting of the first and second heart sounds are usually evident on phonocardiograms, but rarely is the splitting audible. However, even if it is audible it is not characteristic nor pathognomonic of bundle branch block and may occur normally (pages 41 and 55).

Electrocardiogram (Fig 76) —The *QRS* interval is usually widened to 0.12 second or more. Rarely it is as small as 0.10 second (partial or incomplete right bundle branch block). Leads $V_{1,2}$ usually show an *rsR′* pattern with a wide, final *R′*. The peak of the *R′* (time of onset of the intrinsicoid

deflection) occurs 0 07 second or more after the beginning of the QRS, due to the late stimulation of the right ventricle The T wave is downward in these leads Leads $V_{5,6}$ usually show a qRS with a wide prominent S. The augmented unipolar extremity leads and the standard leads vary, depending on whether the heart is horizontal or vertical Lead I usually shows a prominent, wide S, which is why this type of bundle branch block was formerly called the "wide S wave type of bundle branch block"

Laboratory Tests.—Normally the second phase of the second sound, due to the opening of the semilunar valves, precedes the peak of the jugular *v* wave (which occurs just before the opening of the tricuspid valve) by about 0 1 second (page 55) However, in right bundle branch block, the closure of

RIGHT BUNDLE BRANCH BLOCK

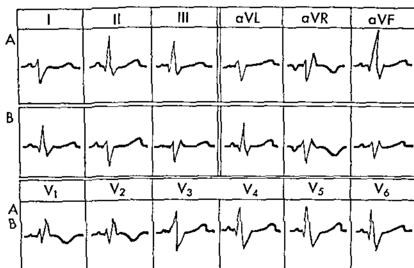


Fig 76 —Right bundle branch block *A*, Shows the pattern when the heart is vertical, *B*, when the heart is horizontal

the aortic valve precedes the closure of the pulmonary valve, so that the peak of the *v* wave is markedly delayed in relation to the beginning of the second sound

Since the contraction of the left ventricle is normal in right bundle branch block, the rise of the carotid pulse tracing has a normal relation to the beginning of the first heart sound, and the carotid incisura occurs normally with the onset of the second sound (page 55)

Diagnosis.—Diagnosis is made from the electrocardiogram. When right bundle branch block complicates myocardial infarction, the electrocardiogram shows the patterns of both the bundle branch block and the myocardial infarct. Thus if anterior infarction is present, the precordial leads show abnormal Q waves and elevated $RS\text{-}T$ segments due to the anterior infarct. In addition the QRS interval is wide, and leads $V_{1,2}$ show qR pat-

terns with a wide, prominent, late *R*, and downward *T* waves, due to the right bundle branch block. When right bundle branch block complicates posterior infarction, the precordial leads show the right bundle branch block, and lead *aVF*, and leads II and III show the patterns of posterior infarction.

When complete *a–v* block is present, a diagnosis of right (or left) bundle branch block should not be made even though the *QRS* complexes are typical of bundle branch block The reason for this is that in the presence of complete *a–v* block, either the right or left bundle of His may act as the idioventricular pacemaker of ventricles (see page 317).

Course and Prognosis.—When right bundle branch block is not due to either pulmonary embolism or myocardial infarction, the prognosis is excellent

Treatment.—The presence of right bundle branch block is not itself an indication for treatment. If underlying heart disease is present, the heart disease should be treated without regard for the bundle branch block

LEFT BUNDLE BRANCH BLOCK

Pathological Physiology.—Because the stimulus cannot spread normally through the left bundle of His, the stimulation of the left ventricle is delayed, so that comparatively marked asynchronism between the contraction of the right and left ventricles occurs However, this does not disturb cardiac function.

Etiology.—Although left bundle branch block can occur in people with normal hearts, it most commonly occurs in patients who have organic heart disease, usually hypertensive cardiovascular disease. However, it may also occur in coronary artery disease, or as a result of quinidine, during acute infections, *etc* It may be transient or permanent, and may appear in every *QRS* complex of the tracing or intermittently

Symptoms —There are no symptoms of left bundle branch block.

Signs.—Since there is asynchronism of right and left ventricular contraction, splitting of the heart sounds can be recorded in the phonocardiogram, but splitting may not be audible In addition, there may be a reduplication of the apical impulse

Electrocardiogram (Fig 77) —The *QRS* interval is widened to 0 12 second or more Precordial leads $V_{1,2}$ show *QS* or *rS* patterns with an elevated *RS–T* and upward *T* Leads $V_{5,6}$ show a wide, notched or slurred *R* wave (without a *q*), and a depressed *RS–T* and downward *T* wave The peak of the *R* in leads $V_{5,6}$ (time of onset of the intrinsicoid deflection) is delayed to 0.09 second or more. The augmented unipolar extremity leads and the standard leads vary depending on whether the heart is horizontal or vertical

Laboratory Tests.—When the heart sounds are recorded simultaneously with the carotid artery pulse, the onset of the carotid pulse is markedly delayed after the onset of the first sound; and the carotid incisura (page 55) occurs after the beginning of the second sound rather than simultaneously with it, due to the slower onset of systole and diastole in the left ventricle than in the right ventricle.

Diagnosis.—Although a palpable reduplication of the apical impulse is suggestive of left bundle branch block, the diagnosis should be made from the electrocardiogram. When left bundle branch block complicates myocardial infarction, it may obscure the patterns of the infarct.

Course and Prognosis.—As a general rule, the presence of left bundle branch block is associated with a decreased life expectancy, but patients may have left bundle branch block and show no signs or symptoms of heart disease for many years

Treatment.—If the bundle branch block is due to drugs, such as quinidine, the drug should be stopped Otherwise, left bundle branch block itself requires no treatment If underlying heart disease is present, the heart disease should be treated without regard for the bundle branch block.

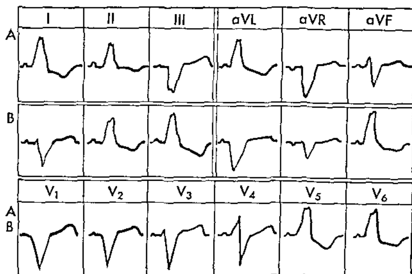


Fig 77 —Left bundle branch block *A*, Shows the pattern when the heart is horizontal, *B*, when the heart is vertical

ABERRANT AURICULO-VENTRICULAR CONDUCTION (THE WOLFF-PARKINSON-WHITE SYNDROME)

Aberrant auriculo-ventricular conduction (anomalous atrio-ventricular conduction, the W P W syndrome) includes the following conditions: the electrocardiogram shows a short *P–R* interval of 0 10 second or less in association with a wide *QRS* complex which may return to normal spontaneously, or after exercise, or after the administration of atropine or amyl nitrite, or during attacks of paroxysmal tachycardia. Young healthy people, especially males, are usually affected

Etiology.—The wide *QRS* pattern superficially resembles that of bundle branch block, but it is now generally believed that the widening of the *QRS*

terns with a wide, prominent, late R, and downward T waves, due to the right bundle branch block. When right bundle branch block complicates posterior infarction, the precordial leads show the right bundle branch block, and lead aVF, and leads II and III show the patterns of posterior infarction.

When complete a–v block is present, a diagnosis of right (or left) bundle branch block should not be made even though the QRS complexes are typical of bundle branch block. The reason for this is that in the presence of complete a–v block, either the right or left bundle of His may act as the idioventricular pacemaker of ventricles (see page 317).

Course and Prognosis.—When right bundle branch block is not due to either pulmonary embolism or myocardial infarction, the prognosis is excellent.

Treatment.—The presence of right bundle branch block is not itself an indication for treatment. If underlying heart disease is present, the heart disease should be treated without regard for the bundle branch block.

LEFT BUNDLE BRANCH BLOCK

Pathological Physiology.—Because the stimulus cannot spread normally through the left bundle of His, the stimulation of the left ventricle is delayed, so that comparatively marked asynchronism between the contraction of the right and left ventricles occurs. However, this does not disturb cardiac function.

Etiology.—Although left bundle branch block can occur in people with normal hearts, it most commonly occurs in patients who have organic heart disease, usually hypertensive cardiovascular disease. However, it may also occur in coronary artery disease, or as a result of quinidine, during acute *infections, etc. It may be transient or permanent, and may appear in every* QRS complex of the tracing or intermittently.

Symptoms.—There are no symptoms of left bundle branch block.

Signs.—Since there is asynchronism of right and left ventricular contraction, splitting of the heart sounds can be recorded in the phonocardiogram, but splitting may not be audible. In addition, there may be a reduplication of the apical impulse.

Electrocardiogram (Fig. 77).—The QRS interval is widened to 0.12 second or more. Precordial leads $V_{1,2}$ show QS or rS patterns with an elevated RS–T and upward T. Leads $V_{5,6}$ show a wide, notched or slurred R wave (without a q), and a depressed RS–T and downward T wave. The peak of the R in leads $V_{5,6}$ (time of onset of the intrinsicoid deflection) is delayed to 0.09 second or more. The augmented unipolar extremity leads and the standard leads vary depending on whether the heart is horizontal or vertical.

Laboratory Tests.—When the heart sounds are recorded simultaneously with the carotid artery pulse, the onset of the carotid pulse is markedly delayed after the onset of the first sound; and the carotid incisura (page 55) occurs after the beginning of the second sound rather than simultaneously with it, due to the slower onset of systole and diastole in the left ventricle than in the right ventricle.

Diagnosis.—Although a palpable reduplication of the apical impulse is suggestive of left bundle branch block, the diagnosis should be made from the electrocardiogram. When left bundle branch block complicates myocardial infarction, it may obscure the patterns of the infarct.

Course and Prognosis.—As a general rule, the presence of left bundle branch block is associated with a decreased life expectancy, but patients may have left bundle branch block and show no signs or symptoms of heart disease for many years

Treatment.—If the bundle branch block is due to drugs, such as quinidine, the drug should be stopped Otherwise, left bundle branch block itself requires no treatment If underlying heart disease is present, the heart disease should be treated without regard for the bundle branch block.

LEFT BUNDLE BRANCH BLOCK

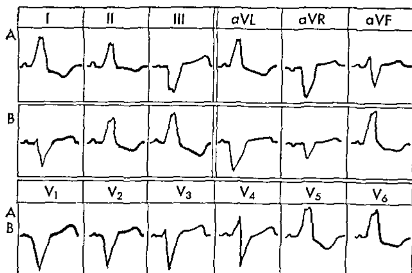


FIG. 77 —Left bundle branch block *A*, Shows the pattern when the heart is horizontal, *B*, when the heart is vertical

ABERRANT AURICULO-VENTRICULAR CONDUCTION (THE WOLFF-PARKINSON-WHITE SYNDROME)

Aberrant auriculo-ventricular conduction (anomalous atrio-ventricular conduction, the W.P.W. syndrome) includes the following conditions: the electrocardiogram shows a short *P–R* interval of 0 10 second or less in association with a wide *QRS* complex which may return to normal spontaneously, or after exercise, or after the administration of atropine or amyl nitrite, or during attacks of paroxysmal tachycardia. Young healthy people, especially males, are usually affected

Etiology.—The wide *QRS* pattern superficially resembles that of bundle branch block, but it is now generally believed that the widening of the *QRS*

is due to the fact that part of the ventricles is stimulated by way of the accessory bundles of Kent (page 316) before the stimulus reaches the ventricles in a normal way through the *a–v* node. However, another explanation is the following: in a normal person, there is a considerable delay in the transmission of the stimulus from the auricles to the ventricles through the *a–v* node *For example, it takes the stimulus about 0 07 second to* travel from the sinus node. (The width of the *P* wave is a measure of this) However, the normal *P–R* interval may reach 0.2 second. Therefore, there is normally a delay of 0 13 second or more in the transmission of the stimulus through the *a–v* node. If a portion of the *a–v* node is able to transmit the stimulus to the ventricles without this delay, the short *P–R* interval and the pattern of aberrant auriculoventricular conduction appear

Symptoms.—The short *P–R* and wide *QRS* in the electrocardiogram cause no symptoms However, palpitation due to attacks of paroxysmal tachycardia, may occur.

Signs.—Physical examination is usually normal, although a small percentage of patients with the syndrome may have organic heart disease.

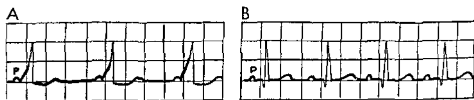


Fig 78 —*A*, Aberrant auriculo-ventricular conduction (Wolff-Parkinson-White syndrome) In *B*, the tracing has become normal

Electrocardiogram (Fig. 78) —The *P–R* interval is 0 10 second or less. When it is very short, part of the *P* wave may merge with the beginning of the *QRS* complex The *QRS* interval is 0 12 second or more wide, but may be shorter, and even within normal limits In those leads in which the *QRS* complex shows an initial *R* wave, the first portion of the *R* is characteristically slurred Neither the standard, unipolar extremity or precordial leads show any characteristic pattern, except the slurring of the first portion of the *R*. When quinidine is administered, the width of the *QRS* tends to become shorter. Digitalis tends to widen the *QRS*.

Diagnosis.—The diagnosis is made from the electrocardiogram with its characteristic short *P–R* interval and slurring of the initial portion of the *QRS* complex The *QRS* interval may or may not be widened beyond 0.12 second.

When aberrant auriculo-ventricular conduction occurs as a complication of acute myocardial infarction, the slurred and widened *QRS* complex may hide or obscure the patterns of the myocardial infarct, and may cause abnormal *Q* waves to disappear. On the other hand, leads III and *aVF* often show a wide *QS*, in the absence of infarction

Course and Prognosis.—The condition is compatible with long life. However, during an attack of paroxysmal tachycardia, the patient may die. The tachycardia may be due to a paroxysmal auricular tachycardia, or paroxysmal auricular fibrillation or auricular flutter. During the tachycardia, the *QRS* width may or may not revert to normal. Attacks of ventricular tachycardia, with markedly aberrant and wide *QRS* complexes, may also occur. However, only about one-half the patients with the short *P–R* and wide *QRS* develop attacks of paroxysmal tachycardia.

Treatment.—No treatment is necessary unless a tachycardia develops. Then quinidine is the drug of choice. Procaine amide may also be helpful.

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Section 4. Systematic Description of Cardiac Abnormalties

Chapter 22

CONGENITAL HEART DISEASE

Introduction.—Until a few years ago, the diagnosis of congenital cardiac lesions was of academic interest only However, with the new methods of surgery available for alleviating and even curing many of the abnormalities, correct diagnosis has become important In most of the congenital lesions which are amenable to surgery, diagnosis can be made from physical examination, routine fluoroscopic or x-ray examination, and electrocardiography However, *angiocardiography, and catheterization of the cardiac chambers are occasionally necessary* For proper understanding of the relations between the various congenital abnormalities, the following brief description of the development of the heart may prove of value

DEVELOPMENT OF THE HEART

The entire development of the heart takes place between the third and the eighth week of embryonic life at which time the heart assumes its adult form, with the exception of the patent foramen ovale and the ductus arteriosus.

The *first major blood vessels that develop are the primitive ventral* aortæ, one on each side. The inferior portions of the aortæ fuse to form a single vascular tube, which is the primitive heart It is continuous with the *paired aortæ above, and the vitelline and umbilical veins below* (Fig 79, A) This cardiac tube then elongates and bends to form an S-shaped loop (Fig 79, B) which can be divided into five parts sinus venosus, primitive atrium, primitive ventricle, bulbus cordis, and truncus arteriosus. The constriction between the atrium and ventricle constitutes the atrial canal, and is the site of the future a-v valves.

Part of the sinus venosus becomes incorporated into the developed right auricle, part persists to form the coronary sinus. The vitelline and umbilical veins return blood to the sinus venosus from the yolk sac and the placenta Blood from the fetal body is carried to the heart by way of paired anterior and posterior cardinal veins which empty into the right and left ducts of Cuvier (Fig 81, B) which in turn empty into the sinus venosus. The right duct of Cuvier and the right anterior cardinal vein develop into the superior vena cava The left duct of Cuvier is incorporated into the left auricle

The Development of the Auricles and the Interauricular Septum (Figs 80, 81) —The atrial canal becomes slitlike, and two thickenings or endocardial cushions project into it, one anteriorly, and one posteriorly, meeting n the midline to form the *septum intermedium,* which divides the atrial canal into two channels, the future mitral and tricuspid valve orifices.

As the primitive atrium develops, it is divided into the right and left auricles (atria) by the *septum primum* which grows downward toward the septum intermedium The open space between the septum primum and

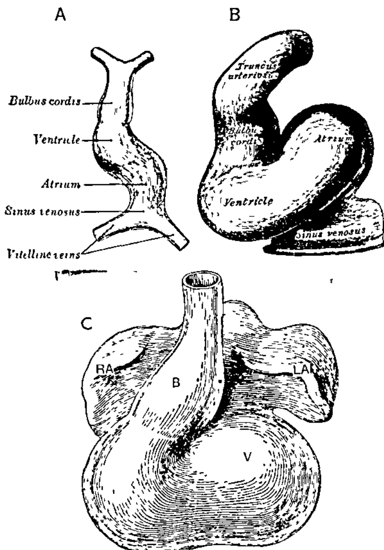


FIG 79 —Diagrams showing stages in the early development of the human heart *A*, The simple tubular structure of the heart *B*, Heart of a human embryo about fourteen days old *C*, A later stage of development when the auricles (atria) have expanded B, Bulbus cordis; LA and RA, left and right auricles (atria); V, common ventricle (From Gray's Anatomy, Lea & Febiger, 26th ed, 1954)

the septum intermedium is known as the *ostium primum* (of Born) The *ostium primum* becomes completely closed when the septum primum meets the septum intermedium, completely dividing the atrium However, at this time a number of small perforations have formed in the upper part of the septum primum. These blend together to form the *foramen ovale* (ostium secundum of Born).

When the septum primum meets the septum intermedium, another septum, the *septum secundum*, grows downward from the upper wall of the right auricle, immediately to the right of the septum primum and later fuses with the septum primum At first it grows anteriorly, then downward and lastly posteriorly, so that its free border becomes concave, the concavity of its margin being directed downward As the septum secundum spreads over the foramen ovale and passes the upper edge of the septum primum, a portion of the septum secundum does not fuse with the septum primum, allowing the foramen ovale to remain between the lower concave edge of the septum secundum and the free edge of the septum primum The foramen ovale acts as a flap valve, allowing blood to pass from the right to the left auricle but not in the reverse direction (Fig 80) This condition persists till birth when the free edges of the septum primum and the septum secundum fuse, and the foramen ovale becomes obliterated The free concave edge of the septum secundum remains as the limbus fossa ovalis However, in at least 10 per cent or more of normal adults, complete fusion of the two septa does not occur and the foramen ovale remains patent in the form of a small opening through which a probe can be passed This has no clinical significance because at birth the pressure in the left auricle becomes greater than that in the right auricle, thus keeping the foramen ovale functionally closed (also see page 404)

Within the right auricular cavity another septum appears, the septum spurium (Fig 81). This lies above the opening of the sinus venosus, and is formed by the fusion of the right and left venous valves, which guard the sinus venosus Below the opening of the sinus, the valves fuse to form a triangular thickening, the spina vestibula These have no clinical significance.

If the development of the heart stops at the stage when the endocardial cushions are forming in the atrial canal, the septum intermedium is not formed, and the ostium primum cannot be closed This causes a defect in the lower portion of the interauricular septum A defect in the upper part of the muscular interventricular septum also results because it cannot meet the absent septum intermedium As a result, the auricles and ventricles communicate with each other through a common *a–v* valve, producing a persistent common auriculo-ventricular ostium

Development may stop after the septum intermedium is formed, but while the septum primum is growing downward, producing a defect in the septal wall just above the septum intermedium, known as a persistent ostium primum. In other examples of interauricular septal defects, abnormalities of both the septum primum and septum secundum are present, resulting in a large free communication between the two auricles. The opening may be near the foramen ovale, which, however, usually can be seen in that part of the septal wall still remaining.

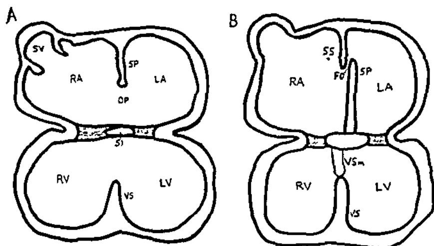


FIG 80—Diagrams showing the development of the interauricular septum. *B*, Is a later stage than *A* FO, Foramen ovale, LA and RA, left and right auricles (atria), LV and RV, left and right ventricles, OP, ostium primum; SP, septum primum; SI, septum intermedium, SS, septum secundum; SV, sinus venosus, VS, interventricular septum; VSm, membranous portion of the interventricular septum.

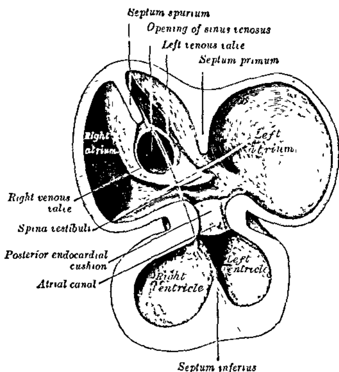


FIG 81.—*A*, Interior of dorsal half of the heart of a human embryo about thirty days old.

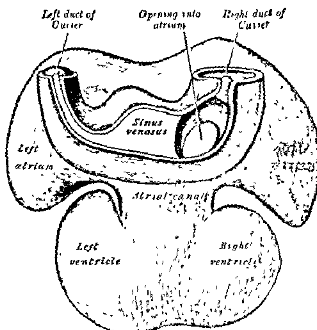


Fig 81 —*B*, Dorsal surface of the heart of a human embryo thirty-five days old

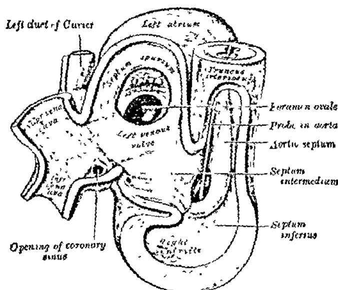


Fig. 81.—*C*, Interior of the right side of the heart of a human embryo about thirty-five days old (From Gray's Anatomy.)

The Development of the Pulmonary Veins.—Four primary veins grow from the lung, two on each side. Each pair unites to form a single vein, and these in turn join in a common trunk which opens into the left auricle. Subsequently, the left auricle expands and incorporates the common trunk and its branches into it, so that in the developed heart, all four veins open separately into the left auricle.

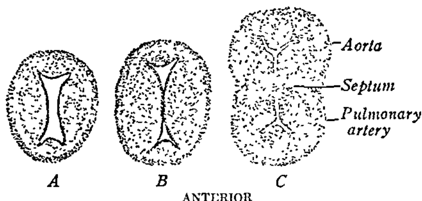


Fig 84 —Diagrams showing the development of the aortic and pulmonary valves. In A, and B, the four endocardial cushions of the truncus arteriosus are shown. C, Shows how the aortic septum forms the aorta and pulmonary artery.

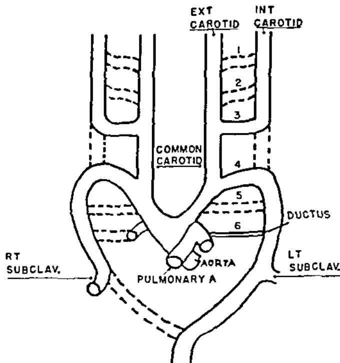


Fig. 85 —Diagram showing the vessels derived from the branchial (aortic) arches. (After Carson and Burford)

The Development of the Branchial (Aortic) Arches (Fig. 85).—As the primitive ventral aortæ run cranially, they turn posteriorly as the first paired branchial (aortic) arch, and continue as the primitive dorsal aortæ. Eventually six such branchial arches arise, connecting the ventral and dorsal aortæ. The sixth arch however, arises directly from the heart and not from the aorta, and when it meets its fellow dorsally, it fuses with it to form a single dorsal aorta. All six arches are not present at the same time, because as the later arches develop, some of the earlier arches disappear, in part, or completely. The first, second and fifth arches disappear completely. The third arch forms the carotid arteries. The fourth arch persists on the left side as the developed aortic arch, and on the right side becomes the innominate artery. The sixth arch forms the pulmonary artery and the ductus arteriosus on the left side. During fetal life the blood that enters the pulmonary artery passes in large part directly from the pulmonary artery through the ductus to the descending aorta, thus short-circuiting the lungs. At birth, with the expansion of the lungs, all the blood from the pulmonary artery enters the lungs, and the ductus ceases to function and begins to become obliterated The process of obliteration, however, may be delayed for even six months or a year or may never occur The fibrous remnant of the ductus is known as the ligamentum arteriosum

Persistence of the right-sided fourth branchial arch, and disappearance of the fourth left-sided arch results in a right-sided aortic arch, which may continue downward on the right side, or may cross over to the left side behind the esophagus at the level of the tracheal bifurcation. If this happens and the left fourth arch persists as a normal left-sided aortic arch, a vascular ring forms around the trachea and esophagus (page 443) A vascular ring can also form if the distal portion of the sixth left aortic arch persists as the ductus arteriosus or ligamentum arteriosum, in association with a right-sided aortic arch which crosses to the left, and in other ways (page 446)

CLASSIFICATION OF CONGENITAL CARDIAC LESIONS

There are numerous classifications of congenital cardiac abnormalities, none of which are completely satisfactory The classification of Abbott, based on the presence or absence of cyanosis, is presented on page 390 The more common congenital abnormalities can be classified according to anatomical disturbance in the following way:

1. Congenital Abnormalities of the Cardiac Muscle
   - Von Gierke's Glycogen Storage Disease, page 401.
   - *Congenital Rhabdomyoma*, page 402
   - Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery, page 402
2. Congenital Displacement of the Heart.
   - Dextrocardia.
     - Dextrocardia Due to Transposition of the Cardiac Chambers (Mirror-Image (Dextrocardia), page 398.
     - Dextrocardia Due to Incomplete Rotation of the Heart, page 399.
     - Dextrocardia Due to Displacement of the Heart Into the Right Chest, page 400

Persistent Truncus Arteriosus, page 449
Absent Aortic Arch, page 460
Transposition of the Aorta and the Pulmonary Artery, page 447.
Idiopathic Dilatation of the Pulmonary Artery, page 451.
Congenital Arteriovenous Fistulas, page 666

7. Congenital Abnormalities of the Major Veins
Abnormalities of the Pulmonary Veins, page 436
Abnormalities of the Vena Cavæ, page 438.
8 Congenital Abnormalities of the Coronary Arteries, page 402

SOME GENERAL CONSIDERATIONS OF CONGENITAL HEART DISEASE

Etiology.—The cause of congenital cardiac lesions is for the most part unknown. Defects in the germ plasm may be a factor in some cases where there is a high familial incidence of the congenital lesion The rôle of uterine and maternal factors has only been recently appreciated, especially since Gregg, Swan and others have shown that if the mother contracts German measles, especially in the first trimester of pregnancy, there is a high incidence of congenital cardiac lesions and congenital cataracts.

Many congenital lesions, such as interauricular septal defects, coarctation of the aorta, *etc.*, can be explained on an ontogenetic basis, namely an arrest or disturbance in the development of the fetus at a particular stage. However, complete explanation of such abnormalities as transposition of the great vessels, or even the tetralogy of Fallot is difficult on the basis of a simple arrest in development For this reason, phylogenetic theories have been developed in which the congenital abnormalities are studied from the viewpoint of comparative anatomy, and are considered to be analogous to structures found in the lower vertebrates Spitzer, for example, considers the various defects associated with a dextroposed aorta as examples not only of an arrest of torsion of the bulbar area of the heart, but of a reopening of the channel analogous to the reptilian right aorta, and the obliteration of the left ventricular aorta.

Symptoms.—Congenital cardiac abnormalities may be present with or without symptoms referable to the cardiovascular system. Dyspnea however, is a common complaint Ordinarily, dyspnea of cardiac origin is due to pulmonary congestion. However, dyspnea often appears in cyanotic lesions such as isolated pulmonary stenosis or the tetralogy of Fallot where the volume of blood in the lungs is much less than normal. In such cases the dyspnea is probably produced by an increased lactic acid content of the blood, resulting from tissue anoxia. Angina pectoris (angina hypercyanotica) may also occur as a result of this chronic anoxemia.

Hemoptysis may occur, especially in the Eisenmenger complex and in interauricular septal defects, where pulmonary congestion is marked. Cerebral manifestations, such as headache, dizziness, syncope and epileptiform seizures, coma and even transient or permanent paralysis of one or more extremities may occur as a result of cerebral anoxia, or of cerebral thrombosis due to secondary polycythemia and slow cerebral blood flow, or as a result of cerebral embolism or cerebral abscess from subacute bacterial endocarditis or from paradoxical embolism (page 392).

Signs.—The most important signs to be looked for are cyanosis and clubbing of the fingers and toes. The mechanisms of cyanosis have already been discussed on page 131 Cyanosis may occur without clubbing, if the cyanosis is of short duration. However, clubbing without cyanosis does not occur as a result of congenital heart disease (page 137).

Cyanosis and clubbing are always strongly suggestive of congenital heart disease, particularly if the history reveals that these signs have been present since childhood When the cyanosis is more marked in the lower extremities than in the upper extremities, this alone suggests an infantile type of coarctation of the aorta, or aortic atresia with a patent ductus arteriosus, or a patent ductus arteriosus with reversed flow due to pulmonary hypertension

In congenital heart abnormalities with cyanosis, the cyanosis is of a central type and due to a venous-arterial, right-to-left shunt. However, if right-sided heart failure occurs, a peripheral type of cyanosis (page 133) may also appear

The presence or absence of cyanosis has been used to classify congenital cardiac lesions in the following way:

1 *Acyanotic Lesions*, including pericardial defects, mirror-image dextrocardia: so-called idiopathic congenital hypertrophy of the heart, left-sided lesions, including subaortic and aortic stenosis, congenital mitral stenosis, coarctation of the aorta, bicuspid aortic valve, abnormalities of the aortic arch, including a right aortic arch, double aortic arch, abnormal origin of the left subclavian artery from the ductus arteriosus or the pulmonary artery, abnormal origin of the right subclavian artery from the descending aorta, anomalous bands and chordæ, congenital *a–v* fistulæ, *etc.* In all these abnormalities, there is no shunting of venous blood into the systemic circulation, so that cyanosis due to the presence of venous blood in the systemic circulation does not occur.

2. *Lesions with Possible, Transient or Terminal Cyanosis* (*Cyanosis Tardive*), including localized interauricular or interventricular septal defects, isolated patent ductus arteriosus, congenital arteriovenous fistula between the ascending aorta and the pulmonary artery (aortic-pulmonary fistula) aneurysm of a sinus of Valsalva, *etc.* In all these abnormalities there are pathways by which venous blood can enter the systemic circulation, but since the systemic pressure is greater than that in the right side of the heart, or in the pulmonary circulation, there is a left-to-right arterio-venous shunt, rather than a right-to-left, venous-arterial shunt, and no unoxygenated blood enters the systemic circulation, unless the right ventricular or pulmonary pressure is temporarily or transiently raised above the systemic pressure. This, however, may never occur.

3. *Cyantic Lesions*, including pulmonary stenosis with a patent foramen ovale, the Eisenmenger complex, tetralogy of Fallot, transposition of the aorta and pulmonary artery, tricuspid, pulmonary, aortic or mitral atresia, complete defects of the cardiac septa producing a three-or two-chambered heart, persistent truncus arteriosus, dextrocardia without situs inversus, *etc.* In all these abnormalities, the defect is of such a degree or is so located that venous blood constantly enters the systemic circulation, producing cyanosis. In some of these abnormalities cyanosis may not appear until adolescence

or even adulthood, as in the Eisenmenger complex. However, in such cases the presence of a right-to-left or venous-arterial shunt is always manifested by a decreased oxygen saturation of the peripheral arterial blood.

Secondary polycythemia may occur in association with the cyanosis. Red blood counts of six and seven million are common, and the count may even exceed twelve million There is also a corresponding increase in hemoglobin, which may be 110, 120 or even 200 per cent The importance of the polycythemia is that it greatly increases the viscosity of the blood causing a sluggish flow and thrombosis in various organs, such as the brain The increased circulating blood volume may also result in epistaxis and hemoptysis

Significant murmurs and thrills may or may not be present This is especially true in infancy and early childhood, where even a patent ductus arteriosus may be present without any murmur or with only a non-specific basal systolic murmur. (The reason for this is that the murmur of patent ductus depends on the relative pressures between the systemic and pulmonary circulations. The marked differences that occur in adult life do not appear in infancy)

Squatting is a common finding in the tetralogy of Fallot and in other conditions where cyanosis is present in association with a decreased blood flow to the lungs.

When the child gets out of breath or feels tired, he sits on his heels with the knees pressed against the chest, the trunk inclining slightly forward. The tibiæ may be almost parallel with the ground. The position is similar to that of a normal person sitting on his heels The child spontaneously adopts this posture, and a very cyanotic child may spend most of the time in this position, even when in bed In later childhood the tendency to squat disappears, although it may persist even in adolescents.

Real benefit is gained by squatting and it can be used as a means of treatment for severe dyspnea or anoxia (see page 393).

Other Associated Abnormalities.—Congenital cardiac lesions may or may ✓ not be associated with other abnormalities. The association of congenital cataract with congenital cardiac lesions as a result of maternal rubella has only recently been pointed out. Rhabdomyoma usually occurs in patients with sclerosis of the cortex of the brain (tuberous sclerosis).

In Marfan's syndrome (arachnodactyly with congenital dislocation of the lens of the eyes), congenital aortic valvular disease, patent ductus arteriosus, dissecting aneurism of the aorta, or localized aneurism of the aorta is common

A persistent ostium atrio-ventricularis communis occurs frequently in Mongolian idiots

Congenital cardiac lesions may cause an inadequate systemic blood flow, resulting in physical underdevelopment. This is especially true of cyanotic lesions, but underdevelopment may even occur in patients with an isolated patent ductus arteriosus. However, an infant or child even with a cyanotic lesion may develop normally. On the other hand, coarctation of the aorta of the adult type is often seen in well-developed males or in females with ovarian insufficiency.

Diagnosis.—Congenital lesions such as patent ductus arteriosus, interauricular septal defects, coarctation of the aorta, subaortic stenosis, the tetralogy of Fallot, tricuspid atresia, right-sided and double aortic arches, dextrocardia, *etc*, can usually be diagnosed by physical examination, history, fluoroscopic and *x*-ray examination and electrocardiogram. However, when a complex or atypical abnormality is present, angiocardiography, venous catheterization and oximetry studies may be necessary. Angiocardiographic findings are described under each individual lesion. A general survey of venous catheterization and oximetry findings is present on page 223

A high pulse pressure with a femoral shock is characteristic of a patent ductus arteriosus On the other hand, in coarctation of the aorta, an almost pathognomonic finding is a femoral pulse which occurs a fraction of a second later than the radial pulse

The presence of a large heart with severe cyanosis and pulmonary congestion suggests transposition of the aorta and the pulmonary artery. A small heart in a cyanosed patient, on the other hand, usually indicates a tetralogy of Fallot or tricuspid atresia.

An enlarged liver in the absence of cardiac failure suggests an abnormality of the tricuspid valve An enlarged liver with presystolic pulsations suggests tricuspid atresia or pulmonary stenosis.

Course and Prognosis.—Infants with cyanotic congenital lesions have a poor prognosis and death often occurs in the first two years of life However, if the infant survives this period, the chances of reaching adolescence or adulthood are good. Infants with noncyanotic lesions have a good chance of reaching adolescence or adulthood.

The most common complication other than heart failure is the development of subacute bacterial endocarditis. The bacteria become engrafted where abnormal currents of blood impinge. Thus, in a patent ductus arteriosus, vegetations usually develop at the pulmonary end of the ductus, and in interventricular septal defects, on the right ventricular wall opposite the septal defect. The only congenital lesion in which subacute bacterial endocarditis is rare is an interauricular septal defect.

An occasional complication of auricular or ventricular septal defects is the development of a cerebral abscess, often solitary, without subacute bacterial endocarditis This may be produced by bacteria which gain entrance to the blood stream during a transient bacteremia but are not filtered out in the lungs, being able to pass directly into the systemic circulation, because of an overriding aorta or a septal defect. Since the cerebral abscess is usually single and accessible to surgical treatment, the condition should be suspected in any patient with congenital heart disease who has abnormal neurological findings.

Paradoxical embolism may also occur in congenital heart disease when a thrombus, formed in the veins, passes through a septal defect and produces systemic embolization. Rare cases have also been reported in which a paradoxical embolism occurred through an otherwise normal patent foramen ovale. In such cases, previous acute pulmonary embolism or chronic pulmonary disease raised the right auricular pressure above that of the left auricle and opened the foramen ovale.

Pulmonary tuberculosis is a rare complication of congenital heart disease. It usually occurs in patients with pulmonary stenosis or the tetralogy of Fallot.

Cardiac arrhythmias are uncommon in congenital heart disease. The presence of auricular fibrillation usually indicates Lutembacher's syndrome (interauricular septal defect and mitral stenosis). Congenital *a–v* block occurs as a result of either an interauricular or interventricular septal defect. It may also occur as an isolated abnormality.

Treatment.—Medical Therapy.—The presence of a congenital cardiac abnormality does not necessarily mean that the child's activities must be curtailed, and it may be much better to deemphasize the cardiac condition than to create a cardiac neurosis at an early age.

When dental extractions are done, prophylactic penicillin should be given as in a case of rheumatic heart disease (page 508) to prevent bacterial endocarditis.

The secondary polycythemia which develops with cyanotic congenital cardiac abnormalities may cause thrombosis, especially cerebral thrombosis. In order to prevent this, the infant or child should not be allowed to become dehydrated, and prophylactic small phlebotomies of 100 to 250 cc. may be advisable, especially if the hematocrit value is 80 per cent or higher.

If a cerebral thrombosis develops, phlebotomy of from 100 to 250 cc. can be done, and a similar volume of saline or of 5 per cent glucose in distilled water given intravenously to dilute the blood further. Anticoagulant therapy with heparin can also be begun, to prevent extension of the thrombus. For children, 25 to 50 mg. of high-potency heparin (50 mg per cc.) can be given intramuscularly or subcutaneously 2 or 3 times a day, checking the coagulation time two and a half hours after each injection by the Lee-White method The coagulation time should rise to 2 or 3 times its previous value. The heparin can be continued for one week or longer.

An adequate fluid intake should be maintained in order to avoid the danger of cerebral thrombosis. An infant should receive 1000 cc of fluid a day, a child of two to eight years, 1500 cc ; a child of eight to twelve, 1500 to 2000 cc , and children over twelve years a minimum of 2000 cc. a day. Adults can receive as much as 3000 or 4000 cc a day. No patient with polycythemia should go more than twelve hours without fluid, and in case of vomiting, diarrhea or excessive heat, the above requirements should be exceeded.

If paroxysmal dyspnea occurs, the infant should be placed in the knee-chest position This may be sufficient to end the attack Morphine sulfate (1 mg per 10 pounds of body weight) hypodermically or by suppository is also very effective Oxygen does not have much value

The same treatment can be used for anoxic spells with loss of consciousness and convulsions

If heart failure occurs, it is treated in the usual way (page 247) Infants and young children with cyanotic abnormalities often develop attacks of paroxysmal dyspnea, even without pulmonary congestion. Taussig recommends morphine sulfate intramuscularly, in a dose of 1 mg. ($\frac{1}{64}$ grain) per 10 pounds of body weight, 0 25 gram of aminophylline intramuscularly, (1 cc of a 2 cc. ampoule) may also be of value in combatting the dyspnea.

Surgical Treatment.—The surgical treatment of coarctation of the aorta, isolated patent ductus arteriosus, vascular rings around the esophagus and trachea, and pulmonary stenosis, *etc*, are discussed under the individual abnormalities.

The Blalock-Taussig Operation.—The operation consists essentially of the establishment of an artificial ductus arteriosus between the systemic and pulmonary circulations Blalock does this by severing the subclavian, innominate, or common carotid artery and anastomosing the proximal end of the artery to the side of the pulmonary artery. In the modification developed by Potts, Smith and Gibson, an artificial ductus is created by connecting the aorta and pulmonary artery directly by means of a side-to-side anastomosis

The purpose of the operation is to increase the oxygenation of systemic blood by bringing unoxygenated blood which has entered the systemic circulation to the lungs for aeration The operation can be done in any congenital cardiac abnormality in which the following factors are present:

1 There is either an auricular or ventricular septal defect with a right-to-left shunt, resulting in the short-circuiting of the flow of blood to the lungs, and resulting in the passage of venous blood directly into the systemic circulation.

2 In addition, there is an inadequate flow of blood to the lungs, either due to the septal defect and the right-to-left shunt, or to pulmonary stenosis or atresia, so that even if all the blood that passes through the lungs were aerated, the available oxygen is not sufficient for the needs of the patient

In addition to these criteria, the following additional conditions must exist for the operation to be successful:

3 A systemic artery of suitable size and length must be available for use in the anastomosis This usually offers no difficulty. In this connection, it is important to determine preoperatively whether a left or right aortic arch is present because the operation should be done on the side opposite to that on which the arch lies. The reason for this is that the best vessel to use for the anastomosis is the subclavian artery arising from the innominate artery When a left aortic arch is present, the innominate artery lies to the right of the sternum, and vice versa

4. There must be present a pulmonary artery to which the systemic artery can be anastomosed. In addition, the pulmonary artery pressure must be lower than the pressure in the aorta and its branches. If the pulmonary artery pressure is greater than the systemic pressure, the flow of blood would be from the pulmonary artery to the systemic circulation, through the artificial ductus, so that no beneficial effect would result from the operation It may be impossible to determine this until the time of operation when the chest is opened and the pulmonary pressure measured directly.

5. The heart must be able to adjust itself to the increased circulation resulting from the operation.

All these conditions are present in the tetralogy of Fallot, and in cases of *tricuspid atresia* The operation is also feasible in patients who have a single ventricle with pulmonary stenosis or atresia. This is relatively common in cyanotic patients with dextrocardia, with or without situs inversus.

The operation can also be performed in patients with a persistent truncus arteriosus, where the circulation to the lungs is by way of the bronchial arteries However, in such cases, there may be no pulmonary artery present for anastomosis This can only be determined at the time of operation.

The operation cannot be used in patients with the Eisenmenger complex, because there is already adequate blood flow to the lungs, and the cause of the cyanosis is pulmonary rather than cardiac. Similarly, the operation cannot be used in patients with an isolated pulmonary stenosis even though cyanosis is present, because, even though an artificial ductus were created, it would only shunt oxygenated blood to the lungs (There is no right-to-left shunt, and no venous blood enters the systemic circulation.) However, the operation could be used in a case of pulmonary stenosis with a patent foramen ovale

After the operation there is usually a rapid improvement in the arterial oxygenation which rises from below 50 per cent to between 70 and 80 per cent The hemoglobin may drop from between 120 and 160 per cent to between 90 and 120 per cent. Most patients have an increased vital capacity and have less cyanosis, clubbing and polycythemia However, some cyanosis usually can be observed on exercise and slight clubbing persists, unless it was minimal before the operation.

In nearly all the successful cases, a continuous murmur can be heard at the site of anastomosis The development of this murmur soon after the operation is an indication of a successful operation Generally, the improvement gained in the first few months after operation is also a good guide to the future of the child

The dangers of the operation include the development of cardiac dilatation and pulmonary edema, cerebral thrombosis, and the occasional development of bacterial endocarditis at the site of the artificial ductus. The optimum age for operation is about five years, although it can be done with little difficulty between the ages of two and twelve years. Below the age of two, the vessels may be too small to manipulate Above the age of twelve, there may be too great a distance between the pulmonary artery and the available systemic artery. The overall mortality from the operation is about 20 per cent

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Chapter 23

CONGENITAL DISPLACEMENTS OF THE HEART AND CONGENITAL ABNORMALITIES OF THE HEART MUSCLE

DISPLACEMENTS OF THE HEART

Dextrocardia.—In dextrocardia, the heart lies in the right thoracic cage. Dextrocardia can be classified in the following way:

A. **Dextrocardia Due to Transposition of the Cardiac Chambers (Mirror-Image Dextrocardia).**—The primitive cardiac tube rotates in the reverse direction of normal when the S-shaped loop is formed (page 379), so that the developed heart lies in the right chest, the apex points to the right, and the "left" ventricle (which pumps arterial blood) lies posteriorly and to the right of the "right" ventricle (which pumps venous blood). The aorta also lies on the right The heart is therefore a mirror-image of normal

Symptoms.—There are no symptoms, and the duration of life is normal Bronchiectasis is a comparatively common complication.

Signs —Cyanosis and clubbing are absent. The apex of the heart lies in the fourth or fifth intercostal space near the right midclavicular line. There are no murmurs nor thrills The heart sounds are heard over the right side of the chest and over the sternum Mirror-image dextrocardia is usually associated with situs inversus, so that the liver will be felt on the left side, and the stomach is on the right side.

Fluoroscopic and X-Ray Examination —The heart is the mirror-image of normal A right aortic arch is a "normal" finding here. When situs inversus is present, the stomach gas bubble is also seen on the right side. The findings in the L A O position are the reverse of a normal R.A.O position, and vice versa.

Electrocardiogram (Fig 86).—The electrocardiogram shows a pathognomonic reversal of the patterns in leads *aVL* and *aVR*, lead *aVR* showing an upward *P*, a tall *R* and an upward *T*, and lead *aVL* showing a downward *P*, a downward *QRS* and a downward *T*. Lead I also shows a downward *P*, downward *QRS* and downward *T* Precordial leads over the right chest are the mirror-image of normal left precordial leads

Diagnosis.—Physical findings of the heart in the right chest, along with the mirror-image *x*-ray picture and signs of situs inversus, and the pathognomonic electrocardiogram make the diagnosis easy.

Occasionally, mirror-image dextrocardia occurs without situs inversus. In most of these cases, there is cyanosis due to associated cardiac abnormalities, such as septal defects, a single auricle or ventricle, *etc.* A left-sided aortic arch may also be present. The electrocardiogram shows the typical patterns of mirror-image dextrocardia in the standard leads and in the

augmented unipolar extremity leads, but the precordial leads to the right of the sternum may show tall *R* waves, due to right ventricular hypertrophy which is present.

Multiple cardiac abnormalities may be present in dextrocardia even if situs inversus is present. In addition, situs inversus may occur in association with a levocardia. In such cases, multiple abnormalities of the heart are also present

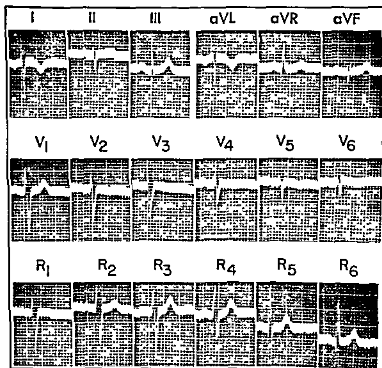


FIG 86 —Dextrocardia with situs inversus Leads R_1 through R_6 were taken across the right chest in the same way as leads V_1 through V_6 were taken across the left chest (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed , 1953)

B. **Dextrocardia Due to Incomplete Rotation of the Heart Around Its Long Axis** —The heart remains on the right side of the chest in its embryonic position as a result of a very early arrest in development. The cardiac chambers have a normal relation to each other, but there is so much counterclockwise rotation present that the apex of the heart is formed by the right ventricle which has been rotated in back of the left ventricle The aorta descends normally on the left side

Incomplete rotation of the heart may occur as an isolated abnormality, but it usually occurs in association with marked abnormalities, such as septal defects In such cases, an exact diagnosis of all the abnormalities present may be impossible.

Signs.—Situs inversus is not present. Cyanosis is often present due to the associated abnormalities. The apex of the heart may be felt near the sternum, and the heart sounds are heard over the sternum and to the right of the sternum.

Fluoroscopic and X-Ray Examination.—Dextrocardia without situs inversus is noted. If the patient is turned into the R. A. O. position to counterbalance the counterclockwise rotation, the cardiac silhouette may become normal.

Electrocardiogram.—The electrocardiogram does not show signs of mirror-imaging. Precordial leads across the left chest may be normal, and show signs of the marked counterclockwise rotation (*qR* patterns in all six precordial leads) or signs of right ventricular hypertrophy may be present, if additional abnormalities are present.

C. **Dextrocardia Due to Displacement of the Heart Into the Right Chest.**—This may occur as a result of absence of the right lung, but usually is the result of acquired pathology, such as pneumothorax, atelectasis, *etc.* In such cases the electrocardiogram is more or less normal, and *x*-ray examination reveals the cause of the dextrocardia.

Course and Prognosis.—Mirror-image dextrocardia with situs inversus usually has an excellent prognosis unless other cardiac abnormalities are present. The prognosis of dextrocardia without situs inversus varies, depending on the severity of the associated cardiac abnormalities, and the degree of cyanosis present.

Treatment.—There is no treatment for the dextrocardia. In patients with dextrocardia who have in addition marked cyanosis due to a single ventricle and pulmonary stenosis or atresia, the Blalock-Taussig operation can be performed (page 394).

Levocardia with Situs Inversus of the Abdominal Viscera.—In this condition, the heart occupies its normal position in the left chest, but the abdominal viscera are transposed. The condition is important because it is amenable to treatment with the Blalock-Taussig operation.

The actual cardiac abnormalities which are present are usually very complicated. Two general types can be described:

A. The left auricle acts as the venous auricle. There is generally a single superior vena cava, also transposed to the left side, and a right-sided aortic arch. The pulmonary veins enter the right auricle.

If the aorta and the pulmonary artery are transposed without any other abnormalities, the circulation would be normal. This usually occurs, but this adaptation, which should be effective, is made ineffective by the additional presence of septal defects and pulmonary stenosis or atresia.

B. The venous auricle lies on the right as normally. There is often a superior vena cava on both sides, the left generally entering the right auricle through the coronary sinus. The aortic arch may be on either side. As in the first type, partial or complete transposition of the aorta and pulmonary artery may be present, an auricular or ventricular septal defect is present, or even a single auricle or ventricle, and pulmonary stenosis or atresia.

These two types can be differentiated by angiocardiography. The electrocardiogram may also be helpful, because P_1 is usually downward

when the venous auricle is transposed and lies on the left side, whereas P_1 is usually upward when the venous auricle lies on the right side. Electrocardiographic signs of right ventricular hypertrophy may or may not be present.

The Blalock-Taussig operation can be used in both types of levocardia with situs inversus of the abdominal viscera, because there is an inadequate blood flow to the lungs in each type. However, the mortality from the operation is high in this condition

CARDIAC DISPLACEMENTS DUE TO OTHER CONDITIONS

Pericardial Defects.—The pericardium may be absent or there may be a large defect on the left side and the adjacent pleura also may be absent, so that the heart and left lung lie more or less in a common pleuro-pericardial cavity. The heart has abnormal mobility and is frequently displaced to the left The condition is symptomless, and is usually discovered as an accidental finding at autopsy.

Ectopia Cordis.—This is a rare condition The heart may lie in the neck, or in the abdomen if there is a diaphragmatic defect, or on the chest wall (pectoral heart) if there is a sternal fissure A patient with a pectoral heart can live several months, and several cases have been reported of adults with an abdominal heart

CONGENITAL ABNORMALITIES OF THE HEART MUSCLE

Glycogen Storage Disease (von Gierke's Disease) —The form of glycogen storage disease which was originally described by von Gierke is characterized by: (a) marked hepatomegaly; (b) fasting hypoglycemia and acetonuria; (c) subnormal increase of blood sugar response to an injection of epinephrine; (d) glucose tolerance test showing a hyperglycemic curve of longer than normal duration and, in contrast; (e) normal galactose and fructose tolerance tests. In these cases the heart is not involved

However, a cardiomegalic type of glycogen storage disease also can occur Here, the glycogen storage is predominantly in the cardiac and striated muscles, although the liver and other viscera are also involved.

The cardiomegalic type of glycogen storage disease is characterized by: (a) marked generalized enlargement of the heart, with early heart failure, usually left-sided; (b) electrocardiographic signs of left ventricular hypertrophy and strain, (c) no fasting hypoglycemia or ketosis, (d) normal glucose tolerance test; and (e) a normal response of the blood sugar to the injection of epinephrine

Cardiac enlargement occurs because of marked infiltration of the heart muscle with glycogen On histological examination, the myocardium has a lacy appearance, the muscle fibers appear vacuolated, and Best's carmine stain discloses numerous glycogen granules in the muscle cells.

Glycogen storage disease can simulate endocardial fibrosis (page 435) because in both conditions left-sided heart failure, electrocardiographic signs of left ventricular hypertrophy and strain, and massive enlargement

26

of the heart can occur. However, the symptoms of glycogen storage disease almost never occur in the newborn, although they almost always appear before the age of six months. In addition, there is a high incidence of consanguinity and a similar disorder in a sibling in glycogen storage disease, in contrast to endocardial fibrosis.

There is no effective treatment.

Rhabdomyoma and Other Tumors of the Heart.—Rhabdomyomas occur as grayish blue nodules in the heart muscle The cells show large vacuolated spaces and spider-like processes, and Best's carmine stain discloses numerous glycogen granules

Rhabdomyomas are principally found in the auricles, especially the left auricle, and in the interventricular septum The tumor frequently occurs in association with tuberous sclerosis of the brain, with multiple skin tumors (adenoma sebaceum) and with abnormalities of the kidneys Some investigators consider rhabdomyoma a congenital malformation and not a true tumor Others consider it a localized form of glycogen storage disease

There are no symptoms and the patient may live to adulthood, unless the tumor interferes with the expulsion of blood from the heart. Sudden death is common.

Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery.—One or both coronary arteries may arise from the pulmonary artery instead of from the aorta, thus nourishing the heart muscle with venous blood When the right coronary artery has this abnormal origin, it does not impair the function of the right ventricle, which it mostly supplies, and the patient lives a normal life

However, venous blood is apparently inadequate for the nourishment of the left ventricle, and when the left coronary artery arises from the pulmonary artery, marked cardiac enlargement may occur The infants may also show episodes of colicky pain with tachycardia, profuse perspiration and cyanosis These attacks often accompany feeding. Signs of right- or left-sided heart failure are usually absent.

The *electrocardiogram* may show signs of left ventricular strain and hypertrophy During an attack, characteristic *RS-T* elevations of myocardial infarction may appear

X-ray examination shows a large left ventricle.

Aberrant origin of the left coronary artery from the pulmonary artery may be difficult to differentiate from endocardial fibrosis (page 435). However, if signs of dyspnea, cough and heart failure are present, endocardial fibrosis is the most likely possibility

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Chapter 24

AURICULAR SEPTAL DEFECTS

The development of the auricles and of the interauricular septum, and the differences between a patent foramen ovale, an interauricular septal defect, including a persistent ostium primum, and a persistent common auriculo-ventricular ostium were described on page 380

Patent Foramen Ovale.—Ten per cent or more of normal people have a small patent foramen ovale which will admit a probe. However, the septal flap which closes the foramen is on the left side of the septum, and since the left auricular pressure is greater than the right, the foramen remains functionally closed, and thus ordinarily has no clinical significance.

However, if the foramen is moderately large, and if the right auricular pressure becomes greater than the left, as for example after a pulmonary embolism, or in cases of cor pulmonale, or during right-sided heart failure, a right-to-left shunt can occur, and more important, a fragment of a thrombus originating in the veins of the lower extremities, or in the right auricle or ventricle, for example, can pass through the foramen and produce embolization of the systemic circulation (paradoxical embolism) In addition, in cases of rheumatic heart disease, if marked enlargement of the right and left auricles occur, a small normal foramen ovale may be stretched so as to produce the signs of a real auricular septal defect

An interesting but rare condition is premature closure of the foramen ovale before birth This prevents the passage of blood from the right auricle to the left auricle so that excess blood enters the right ventricle and is pumped into the lungs, resulting in pulmonary congestion. In addition, the right auricular and right ventricular pressures rise, and the new-born baby may show marked right-sided heart failure, with edema and cyanosis Death occurs in a few days

Interauricular Septal Defect (Auricular or Atrial Septal Defect).—The defect is usually relatively large, averaging 2 to 7 cm. in diameter. The defect may occupy the center of the septum or its upper portion, or the lower portion of the septum may be absent (persistent ostium primum).

Pathological Physiology.—The flow of blood through the septal defect depends on the relative pressures in the right and left auricles. At birth and in early infancy, the right auricular pressure may be greater than the left, so that a right-to-left shunt may occur, venous blood enters the systemic circulation, and the infant may be a blue baby or suffer from attacks of cyanosis which may persist for several days. However, in later life, the left auricular pressure becomes greater than the right, and a left-to-right shunt occurs, with arterial blood entering the pulmonary circulation. Therefore cyanosis is characteristically absent. (The arterial oxygen saturation may be subnormal due to the entrance of some venous blood through the

septal defect in spite of the left-to-right shunt.) If the right auricular pressure becomes high, as during the course of right-sided heart failure, or after a pulmonary embolism, etc , mild or moderate cyanosis may appear, due to the entrance of venous blood into the systemic circulation through the septal defect, but clubbing does not result

The left-to-right shunt brings an excess volume of blood into the right auricle and ventricle, and causes dilatation and eventual hypertrophy of both these chambers The increased output of the right ventricle causes the pulmonary artery pressure to rise, and causes a marked pulmonary artery dilatation. Since much of the blood from the left auricle is shunted to the right side of the heart instead of passing into the left ventricle and aorta, both the left ventricle and aorta remain small Another consequence of the decreased output of the left ventricle is that growth may be stunted

Mitral stenosis (either congenital or rheumatic) is a common accompaniment of interauricular septal defects (Lutembacher's syndrome) The stenosed mitral valve hinders passage of blood from the left auricle to the left ventricle This tends to raise the left auricular pressure and further accentuates the left-to-right shunt through the septal defect However, because of the septal defect, the left auricular pressure does not rise as high as in uncomplicated mitral stenosis, and the marked enlargement of the left auricle, seen in uncomplicated mitral stenosis, does not usually occur

Symptoms.—There are no characteristic symptoms Pressure on the left recurrent laryngeal nerve by the dilated left pulmonary artery may cause hoarseness, pressure on the bronchi may cause a brassy cough. Hemoptysis may also occur because of the increased volume of blood in the pulmonary circuit

Signs.—Occasional patients may show a frail gracile habitus, but this is not characteristic of interauricular septal defects Cyanosis and clubbing are absent The blood pressure is a low normal, and the pulse pressure is small, because of the decreased volume of blood in the systemic circulation

The Heart.—Physical signs of marked right auricular and right ventricular hypertrophy are present A marked precordial bulging may be present, with displacement of the left nipple upward and to the left (page 153), and the apex may be visible, heaving and forceful, and displaced outward even to the anterior axillary line in the sixth intercostal space A forceful systolic pulsation to the left of the lower sternum (page 154) is present

Percussion reveals marked enlargement of the heart to the right and left of the sternum, and an increased area of absolute flatness also to the right and left of sternum (Fig 39, A, page 156)

Thrills and murmurs are variable, and are probably due to the rapid flow of blood through the dilated pulmonary artery rather than through the septal defect A pulmonary systolic murmur, and even a diastolic murmur, due to functional pulmonary insufficiency may be present along with a systolic and even a diastolic thrill The pulmonary second sound is accentuated, and the forceful closure of the pulmonary valve may even be palpated as a sharp shock.

The murmurs are transmitted toward the apex However, if mitral stenosis is also present, a low rumbling apical diastolic and presystolic mur-

mur may be heard. If auricular fibrillation is present, as it very frequently is in cases of interauricular septal defects, only the diastolic murmur will be heard at the apex The murmurs are variable and may suddenly disappear. In other cases, no murmurs may be noted for many years.

A rumbling, apical diastolic murmur may occur in an auricular septal defect (and in other congenital heart abnormalities) in the absence of organic mitral stenosis. The differentiation of this murmur from the murmur due to the Lutembacher syndrome is described on page 168.

Fluoroscopic and X-Ray Examination (Fig 87).—Fluoroscopic and x-ray findings are very characteristic. Marked enlargement of the right auricle, right ventricle, pulmonary artery and hilar vessels are present, along with a small left ventricle and aortic knob, and a comparatively small left auricle.

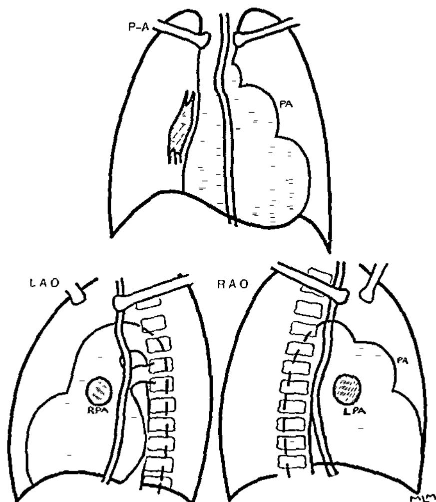


FIG 87.—Interauricular septal defect PA, Pulmonary artery. RPA, LPA, Right and left main branches of the pulmonary artery

P–A Position.—The transverse diameter of the heart is greatly increased, and the heart has a globular appearance. The right auricle is enlarged, and the pulmonary artery segment massively dilated. The aortic knob is inconspicuous. On fluoroscopy, the hilar vessels expand greatly during systole, and abruptly collapse during diastole, producing a hilar dance. This is especially noted on the right side.

R.A.O Position.—Marked enlargement of the right ventricle and pulmonary artery are visible The left pulmonary artery is frequently seen as a large round density within the heart shadow. There may not be much backward displacement of the esophagus by the left auricle even if mitral stenosis is present.

L A O. Position—The enlargement of the right ventricle and right auricle is obvious. The dilated left pulmonary artery, which courses backward to the lungs may appear even larger than the aorta. The right pulmonary artery is often seen as a large round density within the heart shadow.

Angiocardiographic Examination (L A.O. Position).—Although the enlargement of the cardiac chambers and pulmonary artery can be visualized, it is only occasionally possible to demonstrate the spread of the diodrast from the right auricle to the left through the septal defect. The reason that this occurs at all is that the sudden rapid injection of the diodrast may transiently raise the right auricular pressure above the left. Another occasional finding is continued opacification of the right auricle, or reopacification of the right auricle and ventricle, after the left side of the heart is opacified.

Catheterization Studies.—Catheterization of the cardiac chambers may be helpful in doubtful cases. The entrance of oxygenated blood into the right auricle raises its oxygen content significantly above that of the vena cavæ (see page 223). However, a similar increase in right auricular oxygen content over that of the vena cavæ may occur when an anomalous pulmonary vein or veins empty into the right auricle; or with tricuspid insufficiency associated with an interventricular septal defect, or with an arteriovenous fistula between a coronary artery and the coronary sinus (which empties into the right auricle); or with a congenital communication between the left ventricle and the right auricle, or with a persistent common atrioventricular ostium

Rarely, the oxygen content of the right auricle is not higher than in the superior vena cava, even though an auricular septal defect is present The only positive way of making the diagnosis is when the catheter passes from the right auricle through the septal defect into the left auricle and into one of the left pulmonary veins

Circulation Time Tests.—Because of the septal defect there may be a double end-point in the arm-to-tongue circulation time test. The first end-point may occur in a few seconds due to the rapid passage of the decholin or other test substance from the right auricle into the left auricle and the systemic circulation, the decholin short-circuiting the pulmonary circulation. This does not indicate that a right-to-left shunt is present, but it may merely be due to swirling of blood through the septal opening Later, another end-point is obtained when the decholin reaches the tongue by the normal route of right auricle, right ventricle, lungs, left auricle, left ventricle and systemic circulation

In the arm-to-lung test, the passage of ether into the systemic circulation through the septal defect causes paresthesia of the skin of the head and face within a few seconds These reactions however are not specific for interauricular septal defects and also occur with *interventricular septal* defects

Electrocardiogram.—The electrocardiogram shows signs of right auricular and right ventricular hypertrophy. Precordial leads $V_{1,2}$ show tall *R* waves due to right ventricular hypertrophy, and very large biphasic *P* waves, due to right auricular hypertrophy. Right bundle branch block is frequently present In the augmented unipolar extremity leads and standard leads, notched wide *P* waves also appear. The extremity leads show the heart to be vertical with marked clockwise rotation (page 86).

Diagnosis.—A diagnosis can frequently be made from the *x*-ray findings, namely the marked enlargement of the right auricle and ventricle, massive dilatation of the pulmonary artery with a hilar dance, and a small aortic knob. However, if the septal defect is small, and the shunt minimal, the silhouette of the heart may remain normal with only slight prominence of the pulmonary artery.

The patient is frequently a female (less than half the cases are males) and auricular fibrillation or attacks of paroxysmal tachycardia are more common in auricular septal defects than in any other congenital cardiac lesion Interauricular septal defects are also common in patients with arachnodactyly.

Rheumatic heart disease with mitral stenosis or mitral and tricuspid stenosis can mimic the *x*-ray findings of an interauricular septal defect, but in such cases, there is marked posterior displacement of the esophagus by the left auricle in the R A O. position, and the hilar dance is not present.

A patent ductus arteriosus should not be confused with an interauricular septal defect The murmur of a patent ductus is continuous and is higher than that of the septal defect In addition, the heart in patent ductus is *smaller, and the electrocardiogram does not show signs of right ventricular* or auricular hypertrophy

Idiopathic dilatation of the pulmonary artery may present *x*-ray findings of a large pulmonary artery and dilated hilar vessels similar to those of an interauricular septal defect, but *x*-ray signs of marked right ventricular and auricular enlargement are absent and the electrocardiogram is normal (See also page 451).

The Eisenmenger complex without cyanosis can be confused with an interauricular septal defect because in both conditions there is marked dilatation of the pulmonary artery, and right auricular and ventricular enlargement. In a child, differential diagnosis may be impossible unless angiocardiographic or catheterization studies are done. However, cyanosis appears at about puberty in patients with the Eisenmenger complex, whereas cyanosis is absent in auricular septal defects unless heart failure supervenes In addition, auricular fibrillation is commonly present in patients with an interauricular septal defect, and very rare in the Eisenmenger complex.

Course and Prognosis—In spite of the large heart, patients are able to perform their duties for many years, and women, for example, are able to bear many children without difficulty Although rheumatic fever and pneumonia

are common complications, subacute bacterial endocarditis is extremely rare. The average age of death is forty years, death being caused by right-sided heart failure, pulmonary infection or infarction, or intercurrent illness

Treatment.—Many of the auricular septal defects can now be closed surgically. When heart failure occurs, it is treated in the usual way.

Persistent Common Auriculo-Ventricular Ostium (persistent ostium atrioventricularis communis).—The mechanism of production of this abnormality was described on page 381. Physical signs depend on the extent of the auricular and septal defects. If the ventricular septal defect is small, cyanosis and clubbing may be absent, but the peripheral arterial oxygen saturation is decreased because of the entrance of venous blood into the left auricle through the auricular septal defect. However, marked cyanosis may occur. A harsh systolic murmur and thrill are usually present over the precordium

Occasionally, this condition occurs in association with congenital absence of the spleen and situs inversus of the abdominal organs.

Diagnosis is difficult. The condition is commonly present in Mongolian idiots. Death usually occurs before puberty from some intercurrent infection.

Cor Biventriculare Triloculare.—This is a rare condition in which the auricular septum is completely absent, thus producing a three-chambered heart. Cyanosis need not be present, unless other defects, such as transposition of the great vessels, *etc.*, are also present

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Chapter 25

VENTRICULAR SEPTAL DEFECTS

The development of the ventricles and of the interventricular septum was described on page 384 A defect of the interventricular septum may occur as an isolated abnormality, but more commonly is found in association with dextroposition of the aorta and abnormalities of the pulmonary valve and artery.

ISOLATED INTERVENTRICULAR SEPTAL DEFECT

(Roger's Disease)

The defect usually occurs in the membranous portion of the ventricular septum just beneath the aortic cusps, and is due to failure of the bulbar septum to fuse completely with the ventricular septum (see page 385). However, the defect may occur lower in the muscular portion of the septum The cause of such defects is unknown Regardless of the location of the defect, it may vary from a pinhead-sized opening to one large enough to admit the thumb Since the defect opens into the right ventricle beneath one of the cusps of the tricuspid valve, the valve cusp may become deformed, producing tricuspid insufficiency in association with the septal defect

Pathological Physiology —Regardless of the location of the defect, the left ventricular pressure is greater than the right, so that a left-to-right shunt occurs and cyanosis does not appear, if the defect is small, the volume of the shunt may be minimal. However, if the volume of the shunt is large, the right ventricle dilates and hypertrophies to accommodate the excess blood and pulmonary congestion will occur

Symptoms —There are no symptoms of an uncomplicated ventricular septal defect.

Signs —Cyanosis and clubbing are absent.

The Heart.—Physical examination usually does not reveal enlargement of the heart The most characteristic finding is a loud harsh systolic murmur, almost always with a systolic thrill, maximal at the third or fourth intercostal space, just to the left of the sternum and transmitted widely over the precordium and back A diastolic murmur may be heard along the left sternal border. This is probably due to functional pulmonary insufficiency

Fluoroscopic and X-Ray Examination —The heart is usually normal in size The pulmonary artery is prominent. In cases with a large left-to-right shunt, enlargement of the right ventricle may occur, and the hilar vessels may become prominent.

Angiocardiographic Examination.—It is possible in about one-third of the patients to demonstrate either early opacification of the left ventricle while the right heart is visualized, or reopacification of the right ventricle or pulmonary artery later, when the left side of the heart is visualized.

Catheterization Studies.—Because of the left-to-right shunt, the oxygen content of the right ventricle is greater than that of the right auricle (see page 223) The right ventricular pressure may be normal or increased. However, similar values may be obtained in a patient with a patent ductus arteriosus and an associated pulmonary insufficiency.

Electrocardiogram.—The electrocardiogram may be normal. Occasionally intraventricular conduction disturbance or complete *a–v* block occurs if the septal defect has interrupted the bundle of His or its branches Large biphasic deflections may occur in the standard and unipolar extremity leads, but this is not pathognomonic of ventricular septal defects.

Circulation Time Tests.—Normal values may be obtained. However, because of the septal defect, results similar to that in an interauricular septal defect (page 221) may occur

Diagnosis—Congenital aortic or subaortic stenosis may simulate an isolated interventricular septal defect, because both conditions may show a harsh systolic murmur along the left sternal border and minimal cardiac enlargement, and angiocardiographic studies or catheterization studies may be necessary for differential diagnosis However, in aortic and subaortic stenosis, there is a tendency for left ventricular hypertrophy to occur, whereas in ventricular septal defects, enlargement of the right ventricle occurs In addition, the pulmonary artery is not prominent, the hilar markings are not prominent (unless left-sided heart failure is present) and right ventricular hypertrophy is absent

Pulmonary stenosis can also simulate a ventricular septal defect However, the lung fields are abnormally clear in pulmonary stenosis

An auricular septal defect may also simulate a ventricular septal defect However, if a murmur and thrill are present, they are found higher, over the pulmonary artery

Course and Prognosis—The septal defect does not cause undue cardiac strain, but acute or subacute bacterial endocarditis is a frequent complication The site of implantation of the bacteria is the wall of the right ventricle, opposite the septal defect, where the blood streaming through the defect, strikes the right ventricle. Pulmonary infarction may therefore be the first sign of the right-sided bacterial endocarditis. Death usually occurs in most patients before the age of forty years.

Treatment.—There is, as yet, no treatment for the septal defect

THE EISENMENGER COMPLEX

Interventricular Septal Defect Associated with Dextroposition of the Aorta.

In the Eisenmenger complex, there is not only a defect of the membranous portion of the interventricular septum, but there is also a dextroposed aorta which overrides both the right and left ventricles. The pulmonary artery may be normal or markedly dilated. The abnormality is produced both

by failure of the bulbar and ventricular septa to meet, and by inadequate rotation of the aorta to the left (see page 385). The cause of the dilatation of the pulmonary artery and its branches is unknown

Pathological Physiology.—The physiological disturbance is similar to that which occurs in a simple defect of the membranous portion of the interventricular septum However, because the aorta overrides both ventricles, it receives a mixture of venous and arterial blood The shunt of blood through the septal defect is usually from left-to-right However, sclerotic changes in the pulmonary vessels and an increased pulmonary resistance may cause pulmonary hypertension so that a right-to-left shunt may also occur

Ordinarily the presence of venous blood in the arterial system is not sufficient to produce visible cyanosis although the peripheral arterial oxygen content is decreased However, the pulmonary hypertension eventually becomes so marked that the pressure within the right ventricle may exceed the systemic blood pressure, causing a marked right-to-left shunt with severe cyanosis and clubbing The Eisenmenger complex is practically the only congenital abnormality in which cyanosis appears in spite of the presence of a large pulmonary artery and an adequate circulation to the lungs

Symptoms —The most common symptoms are dyspnea, and hemoptysis, which may be massive The hemoptysis is due to the large volume of blood in the lungs and to the pulmonary hypertension However, it is not pathognomonic of the Eisenmenger complex, and may occur in interauricular septal defects, in acquired mitral stenosis, *etc* When the pulmonary artery is dilated, pressure on the left recurrent laryngeal nerve may cause hoarseness, and pressure on a bronchus may produce a brassy cough

Signs.—Cyanosis and clubbing may be absent in infancy and childhood, and usually appear first during the period of adolescence. However, both cyanosis and clubbing may both appear early in infancy

The Heart.—Physical examination of the heart may reveal normal findings although slight enlargement of the right and left ventricles may be present However, the pulmonic second sound may be markedly accentuated because of the pulmonary hypertension The flow of blood through the dilated pulmonary artery may produce a loud, harsh, systolic murmur, associated with a thrill, in the pulmonary area, transmitted widely over the precordium Rarely, the septal defect, which lies just beneath the aortic cusps, so deforms one of the cusps that aortic insufficiency develops, with a systolic and diastolic murmur along the left sternal border, and with characteristic peripheral signs of aortic insufficiency (see page 535) However, a diastolic murmur along the left sternal border may be due to functional pulmonary insufficiency This can be differentiated from aortic insufficiency because the peripheral signs of aortic insufficiency are absent.

Fluoroscopic and X-Ray Examination.—When the pulmonary artery and its branches are normal, the shape of the heart is not distinctive and resembles that of an uncomplicated interventricular septal defect (page 411)

When the pulmonary artery and its branches are dilated, the globular shape of the heart resembles that of an interauricular septal defect and shows the following characteristics (Fig 88)

When the pulmonary artery and its branches are dilated, the shape of the heart resembles that of an interauricular septal defect and shows the following characteristics:

P–A Position —Marked enlargement of the pulmonary artery segment is present. The hilar vessels are enlarged and prominent, and may show a hilar dance

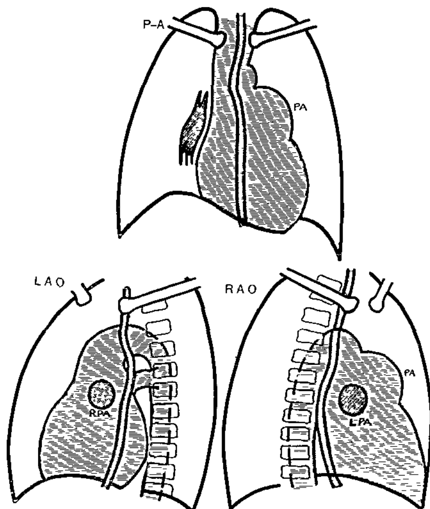


Fig 88 —The Eisenmenger complex

R A O. Position —Enlargement of the pulmonary artery is visible. The right ventricle however is only moderately enlarged.

L.A O. Position.—A large pulmonary artery is visible in association with moderate enlargement of the right and left ventricles

A diagnosis of the overriding aorta can be made in the *L A.O.* position, if the following conditions are present:

1. The patient has congenital heart disease of the cyanotic type.

2 There are clinical and electrocardiographic signs of right ventricular hypertrophy.

3 In spite of the presence of right ventricular hypertrophy, the ventricular silhouette in the *L A O* position resembles a normal heart and does not project anteriorly beyond the root of the aorta (Fig 89). This is in contrast to the ordinary case of right ventricular hypertrophy where the

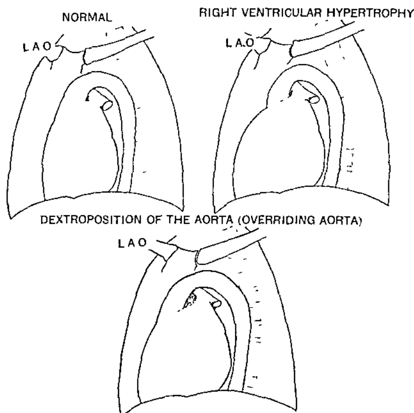


Fig 89 —Characteristics of dextroposition of the aorta (overriding aorta) (after Henry) See text for details

right ventricular silhouette shows a marked bulge anteriorly beyond the root of the aorta (Fig 89)

4 The anterior margin of the ascending aorta must be clearly identified. This last criterion is important because this portion of the aorta in an infant is often hidden by the thymus or obscured by axillary folds.

The overriding aorta can be identified in the Eisenmenger complex, the tetralogy of Fallot, transposition of the aorta and pulmonary artery, *etc.*

Angiocardiographic Examination (L A O. Position) (Fig 91, *B*).—The *aorta is opacified along with the right ventricle and the pulmonary artery*

in about two seconds, indicating that a septal defect is present with a dextroposed, overriding aorta. The large dilated pulmonary artery differentiates the Eisenmenger complex from a tetralogy of Fallot where the septal defect and the dextroposition of the aorta is associated with pulmonary stenosis. Reopacification of the right ventricle, through the septal defect, may also occur later, when the left side of the heart is opacified

Early opacification of the aorta can occur in conditions such as pulmonary stenosis with a patent foramen ovale and a right-to-left shunt, auricular septal defects, and patent ductus arteriosus with a right-to-left shunt, where an overriding aorta is *not* present. In such cases, however, the dye will be noted in the left auricle before it reaches the aorta (The left ventricle may not become opacified even though a large amount of dye has passed through it)

Catheterization Studies —Because of the ventricular septal defect, and the left-to-right shunt that is usually present, the oxygen content of the right ventricle is significantly higher than that of the right auricle, just as in an isolated ventricular septal defect (page 223). However, the pressures in the right ventricle and pulmonary artery are increased and equal to the pressure in the aorta

The most accurate method of diagnosing the overriding aorta which is present is to find that the catheter has passed directly from the right ventricle into the aorta (With rare exceptions, the presence of a right-sided aortic arch in a *cyanotic* patient also indicates that the aorta arises completely or partly from the right ventricle)

Oximetry and Exercise Tests.—Because of the dextroposed and overriding aorta, the peripheral arterial oxygen saturation is decreased. During exercise, the oxygen saturation of peripheral arterial blood falls because of the increased utilization of oxygen by the tissues and the greater volume of venous blood pumped into the aorta from the right ventricle (In a normal person the arterial oxygen saturation remains unchanged after exercise, page 223) However, because of adequate blood supply to the lungs, the pulmonary circulation increases sufficiently to meet the respiratory demands of exercise, and the amount of oxygen consumed per liter of ventilation rises, just as in a normal person This is in direct contrast to the effect of exercise in a patient with an inadequate blood supply to the lungs, as in the tetralogy of Fallot, where the pulmonary obstruction limits the effective pulmonary blood flow, and the amount of oxygen consumed per liter of ventilation falls instead of rising. This test has been used to determine whether the patient is a suitable candidate for the Blalock-Taussig operation, because the operation is effective only if there is an inadequate blood supply to the lungs.

Circulation Time Tests —Values are similar to those obtained in the tetralogy of Fallot (page 222).

Electrocardiogram —The electrocardiogram is not distinctive and is similar to tracings obtained in isolated ventricular septal defects (page 412)

Diagnosis.—The presence of a loud systolic murmur in the pulmonary area with a loud pulmonary second sound, in a patient with moderate or marked cyanosis and clubbing, moderate enlargement of the heart and pulsating hilar vessels, and a history of hemoptysis, is very suggestive of the Eisenmenger complex.

When the Eisenmenger complex exists with a normal pulmonary artery and no cyanosis, the clinical picture resembles that of an isolated interventricular septal defect, and cases have been reported where it has been difficult to determine whether the aorta was dextroposed. When cyanosis is present, and the pulmonary artery is not markedly dilated, the Eisenmenger complex resembles the tetralogy of Fallot, and angiocardiography or catheterization studies may be necessary for the differential diagnosis When the pulmonary artery and its branches are large and dilated, the clinical picture resembles that of an interauricular septal defect, but cyanosis is rare in an interauricular septal defect unless right-sided heart failure has occurred. X-ray examination in the *L A O.* position will show the overriding aorta

Course and Prognosis —Most patients with an Eisenmenger complex die by the age of forty years either from heart failure, pulmonary infection, acute or subacute bacterial endocarditis or intercurrent illness

Treatment —There is no effective treatment.

THE TETRALOGY OF FALLOT

Interventricular Septal Defect Associated with Dextroposition of the Aorta and Pulmonary Stenosis or Atresia

The four characteristics of the tetralogy of Fallot are:

1. A defect of the membranous portion of the interventricular septum

2 Dextroposition of the aorta which overrides both the right and left ventricles.

3 Pulmonary stenosis. This is usually a stenosis of the infundibulum of the right ventricle, which is either narrowed throughout, or exists as a "third ventricle," separated from the right ventricle, which lies below it, by a constricting opening. However, a valvular type of pulmonary stenosis (page 425) may be present instead

Associated with this is a thin-walled, narrow, pulmonary artery, and an abnormal pulmonary valve, which is bicuspid, defective or stenosed The ductus arteriosus is closed. In extreme cases, pulmonary atresia occurs (page 422).

4 Right ventricular hypertrophy

The tetralogy of Fallot is due to incomplete rotation and division of the truncus arteriosus, which produces the small pulmonary artery and the dextroposed aorta, and to an arrest of the normal process of absorption and *integration of the bulbus cordis into the right ventricle* This produces the so-called third ventricle and the pulmonary stenosis, according to Keith. An associated abnormality in about one-fourth of the cases is the presence of a right aortic arch (Corvisart's disease). According to Spitzer, both the overriding aorta and the right aortic arch are due to the failure of development of the normal left aortic arch, and the reopening of the right aortic arch, as occurs in reptiles.

Pathological Physiology —Because of the overriding aorta, the arterial system receives a mixture of venous and arterial blood. This causes a decreased peripheral arterial oxygen saturation, which is further aggravated

by the fact that the pulmonary stenosis prevents adequate pulmonary circulation and aeration of the venous blood. As a result, cyanosis and clubbing develop early in infancy

Right ventricular hypertrophy develops because of the increased resistance offered by the pulmonary stenosis to the outflow of blood from the right ventricle In addition, the shunting of blood from the right ventricle into the systemic circulation increases the venous return to the right ventricle, which dilates and hypertrophies to receive and propel the increased volume of blood

Symptoms —Because of the constant anoxemia, the infant or child usually eats poorly and gains weight slowly. Dyspnea on exertion, or attacks of paroxysmal dyspnea are common, and the infant often assumes a characteristic squatting position until his respiratory distress subsides. However, this squatting position is not pathognomonic of the tetralogy of Fallot and occurs in any congenital lesion where there is inadequate circulation to the lungs.

Fainting spells and even convulsions are common because of the inadequate oxygen supply to the brain Cerebral thrombosis and hemiplegia may occur because of the marked secondary polycythemia and hemoconcentration which is usually present

Signs —The child is usually thin and underdeveloped because of the constant anoxemia Marked cyanosis is present, especially noted on the lips, mucous membranes of the mouth and the conjunctivae. Clubbing is usually very prominent. The blood pressure tends to be low, and may be difficult to record because the pulse pressure is also small.

The Heart —On physical examination the heart may not appear enlarged However, there may be precordial prominence, displacement of the left nipple, and a palpable systolic expansile pulsation just to the left of the lower sternal region, because of the right ventricular hypertrophy The pulmonary second sound is usually weak because of the pulmonic stenosis Occasionally it may appear to be loud This is due to transmission of the aortic second sound to the left of the sternum A reduplicated pulmonic second sound, however, does not occur.

The flow of blood through the stenotic pulmonary valve produces a systolic murmur and thrill along the left sternal border at or near the third intercostal space The quality of the murmur has been described as a squirt, rather than the blowing quality of the murmurs of acquired heart disease. The murmur is usually not transmitted to the neck, and is usually heard better on lying than on standing. When the flow of blood through the pulmonary orifice is minimal as in marked pulmonary stenosis or atresia, no murmurs may be present.

Fluoroscopic and X-Ray Examination (Fig. 90).—The shape of the heart is frequently distinctive

P–A Position.—The cardiac silhouette appears small, but the apex is blunt and lifted above the diaphragm, giving the appearance of a wooden shoe (*coeur en sabot*). The pulmonary artery segment is concave because of the pulmonary stenosis, the hilar shadows inconspicuous, and the lung fields are remarkably clear, due to the small volume of blood circulating through the lungs. In some cases, the hilar vessels may appear engorged due to the

development of collateral circulation However, on fluoroscopy, expansile pulsations of the vessels are not present The aortic knob is not prominent because of the overriding aorta A right aortic arch is frequently present

R.A.O. Position.—The right ventricular contour is prominent, but there is no fullness in the region of the pulmonary artery segment

L.O.A. Position.—Enlargement of the right ventricle is present. The aortic window is usually clear because of the small pulmonary artery.

The overriding aorta can be seen (page 414).

Angiocardiographic Examination (L.A.O. Position) (Fig. 91, *A*).—The overriding aorta is visualized in about two seconds along with the right ventricle and the small pulmonary artery. The left ventricle may or may not be opacified at the time the right ventricle is. The pulmonary stenosis is well visualized The right ventricle may become reopacified in about six seconds when the left side of the heart is visualized

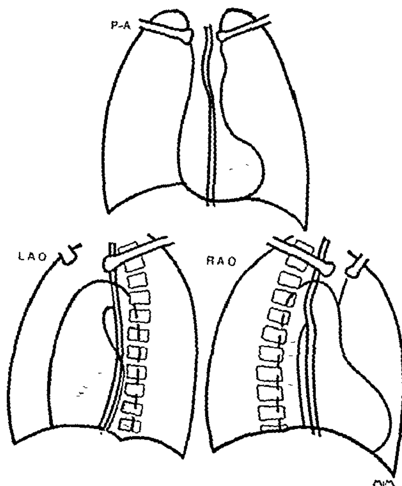


Fig. 90 —Tetralogy of Fallot.

Catheterization Studies.—The pressure in the right ventricle is higher than that in the pulmonary artery because of the pulmonary stenosis The oxygen content of the right ventricle is similar to that of the right auricle unless a left-to-right shunt occurs through the septal defect. This will raise the oxygen content of the right ventricle above that of the right auricle.

Oximetry.—The oxygen saturation of peripheral arterial blood is low because of the entrance of venous blood into the overriding aorta. On exercise, it drops markedly lower due to the inability of the heart to pump

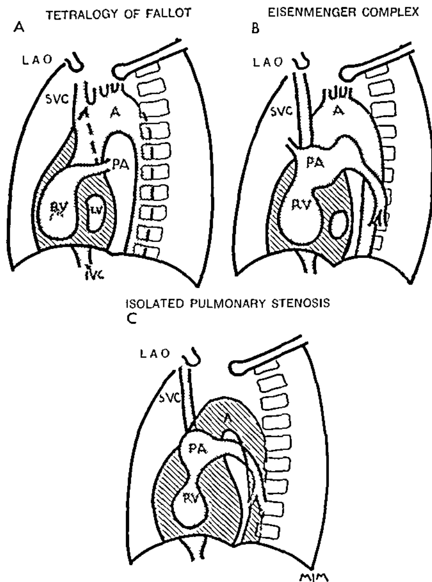


FIG. 91—Angiocardiograms taken in the L.A.O. position *A*, Tetralogy of Fallot. *B*, Eisenmenger complex *C*, Isolated pulmonary stenosis

enough blood through the lungs to replace the oxygen which is being consumed by the muscles at an accelerated rate In addition, the amount of oxygen consumed per liter of pulmonary ventilation falls because the pulmonary stenosis prevents an increased flow of blood to the lungs, unlike in cases of simple septal defects or in cases of Eisenmenger complex (pages 412 and 416)

Circulation Time Tests—Normal values may be obtained. However because of the presence of an overriding aorta and a septal defect, the test substance may be shunted into the systemic circulation directly from the right auricle, short-circuiting the lungs. Thus, with the arm-to-tongue circulation time, a double end-point may occur. The first end-point is noted within ten seconds, the second end-point at the regular time. When the arm-to-lung circulation time is done, the ether passes directly into the systemic circulation and produces paresthesias of the face, head and extremities within a few seconds

These findings are not pathognomonic of the tetralogy of Fallot. Similar results may occur in the Eisenmenger complex, in uncomplicated ventricular septal defects, in interauricular septal defects (page 407), and in any lesion with a large septal defect.

Electrocardiogram.—The electrocardiogram usually shows signs of right auricular and right ventricular hypertrophy, namely large P waves and tall R waves in precordial leads $V_{1\ 2}$.

Diagnosis—The tetralogy of Fallot is by far the most common congenital lesion in which cyanosis dates from infancy, and the diagnosis can thus be suspected on this ground alone. Physical examination may not be characteristic, but there may be signs of right ventricular hypertrophy, and a systolic murmur along the left sternal border. The pulmonary second sound may be faint or loud, but it is not reduplicated A reduplicated second sound would indicate forceful asynchronous closure of an aortic and pulmonary valve, whereas the small volume of blood ejected by the right ventricle precludes forceful closure of the pulmonary valve A diagnosis can sometimes be made from x-ray examination alone if the characteristic findings of a small boot-shaped heart, absent pulmonary artery segment, minimal hilar markings, extremely clear lung fields and right ventricular hypertrophy are present, with or without a right aortic arch

In early infancy, complete transposition of the aorta and pulmonary artery may simulate the tetralogy of Fallot, but in a case of transposition, marked cardiac enlargement occurs as the infant grows, whereas in the tetralogy, the heart remains small In addition, the lungs show marked congestion in a case of transposition

Tricuspid atresia may also simulate the tetralogy. However, in tricuspid atresia, there is also defective development of the right ventricle, which results in left ventricular hypertrophy with characteristic x-ray and electrocardiographic findings (page 430).

When the hilar markings are marked in a case of tetralogy, differentiation from the Eisenmenger complex may be impossible except by angiocardiography or catheterization studies

In older patients, congenital isolated pulmonary stenosis with a patent foramen ovale may simulate the tetralogy because cyanosis, a systolic pul-

monary murmur, and right ventricular hypertrophy appear. However, on *x*-ray examination, post-stenotic dilatation of the pulmonary artery occurs, so that the boot-shaped heart of the tetralogy does not appear.

Tetralogy of Fallot with Pulmonary Atresia (Pseudotruncus Arteriosus).—In this condition, the pulmonary artery is absent. The circulation to the lungs is by way of bronchial arteries or through a patent ductus arteriosus

The term, *pseudotruncus arteriosus*, is commonly applied to the tetralogy of Fallot with pulmonary atresia In true truncus arteriosus (page 449), the aortic trunk arises from both the right and left ventricles and gives off the right and left pulmonary arteries The pulmonary arteries are large and there is a good pulmonary blood flow. In pseudotruncus, there is no main pulmonary artery because the pulmonary valve is absent. The lungs are therefore supplied with blood either via a patent ductus or by bronchial arteries

In the tetralogy of Fallot with pulmonary atresia, all the blood which enters the right ventricle is pumped into the aorta. The blood therefore reaches the lungs by way of a patent ductus arteriosus. If the ductus closes spontaneously, death will occur unless collateral circulation to the lungs has been able to develop by way of the intercostal or internal mammary arteries, or by way of the bronchial arteries which may become greatly enlarged

The clinical picture of the tetralogy of Fallot with pulmonary atresia is similar to that of the usual tetralogy. However, a continuous murmur may be heard in the pulmonary area This is usually due to large, tortuous bronchial arteries rather than to a patent ductus arteriosus. It is more localized than the murmur of a patent ductus, and may be heard on the right side as well as on the left, depending on the location of the enlarged bronchial arteries.

Pulmonary atresia cannot be recognized by physiological tests However, angiocardiography may reveal the absent main pulmonary artery.

In rare cases, the tetralogy of Fallot may occur with atresia of the left pulmonary artery, or atresia of the right main pulmonary artery if dextrocardia is also present.

Atresia of the left main pulmonary artery can be diagnosed on the basis of the following:

1 The left side shows a marked decrease of pulmonary vascular markings, which are exaggerated on the right side. In addition, the right side shows a greatly dilated main pulmonary artery A hilar dance may even be present on the right side

2 The systolic murmur of the tetralogy of Fallot, if present, is heard best in the right chest and under the right clavicle

Course and Prognosis.—In spite of the marked cyanosis and decreased functional capacity of the heart, patients may live well into adulthood, although death usually occurs during childhood. Common causes of death are bacterial endocarditis, cerebral thrombosis, or intercurrent infections.

Treatment.—Although there is no cure for the tetralogy of Fallot, the clinical condition of the patient can often be remarkably improved by increasing the blood supply to the lungs by means of the Blalock-Taussig operation (page 394).

An alternate method of treatment would be to perform pulmonary valvulotomy and resection of the infundibulum of the right ventricle, in an attempt to relieve the pulmonary stenosis. This procedure is not completely satisfactory, because the ventricular septal defect is still present.

COR TRILOCULARE BIATRIUM

In this abnormality the ventricular septum never develops. Instead there is a single ventricle into which the right and left auricles open, producing a three-chambered heart (cor triloculare biatrium). There is also a rudimentary outlet chamber above the ventricle, representing a persistent bulbus cordis. There are three types of cor triloculare biatrium:

1 The first type shows a normal sized aorta which arises from the common ventricle. A small pulmonary artery arises from the rudimentary chamber The clinical picture is similar to tricuspid atresia, and the Blalock-Taussig operation is of value.

2 In the second type, there is transposition of the great vessels so that a small aorta arises from the rudimentary chamber and a normal-sized pulmonary artery arises from the common ventricle As a result, a large quantity of blood is brought to the lungs for oxygenation so that even though there is constant mixture of venous and arterial blood in the heart, cyanosis may not be present until terminal heart failure develops Murmurs are variable. X-ray examination in such cases shows a large heart which resembles the water-bottle shape of pericardial effusion Prominent hilar markings are present

Catheterization studies reveal that the oxygen saturation of the "right" ventricle is identical with that of the peripheral blood, indicating that there is only one ventricle

The electrocardiogram may show large, biphasic deflections in the standard and unipolar extremity leads

There is no effective treatment Death usually occurs during childhood, but the patient may live to adulthood

3 In the third type, both vessels arise from the rudimentary chamber and are of approximately the same size The clinical picture is not distinctive.

COR BILOCULARE

The auricular septum may also be absent in addition to the ventricular septum, producing a cor biloculare. This abnormality is not compatible with life for more than a few months

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Chapter 26

CONGENITAL VALVULAR AND ENDOCARDIAL LESIONS, AND CONGENITAL ABNORMALITIES OF THE VEINS

CONGENITAL PULMONARY STENOSIS

CONGENITAL pulmonary stenosis with an intact ventricular septum may occur as an isolated abnormality. Or, it may be associated with a patent foramen ovale, or with an auricular septal defect, or with a ventricular septal defect Pulmonary stenosis also occurs as part of the tetralogy of Fallot (page 417)

The pulmonary stenosis may involve the pulmonary valve, or the infundibulum of the right ventricle, or both structures may be involved The clinical picture of pulmonary *valvular* stenosis is slightly different from pulmonary *infundibular* stenosis

Congenital Pulmonary Valvular Stenosis.—This is the most common type of pulmonary stenosis The stenosis is produced by a dome-shaped diaphragm which has a small opening, a few millimeters in diameter, in its center The outlines of the valve leaflets can usually be seen within the diaphragm, which is produced by fusion of the leaflets, possibly as a result of a fetal endocarditis. Occasionally, the stenosed leaflets are thickened and deformed, or bicuspid.

Pathological Physiology.—Right ventricular hypertrophy occurs in an attempt to overcome the obstruction to the flow of blood from it. This in turn causes right auricular enlargement

Symptoms.—There may be no symptoms until the onset of heart failure or of subacute bacterial endocarditis. In some cases, dyspnea on effort may occur, due to the inadequate flow of blood to the lungs.

Signs.—Some children may show a bloated, full, "moon-facies." The cause of this is unknown There is no cyanosis, but marked pallor may be present.

In the late stages of the condition, when right-sided heart failure has occurred, a peripheral type of cyanosis, due to stasis, may develop. However, clubbing does not appear

The pulse pressure is small, due to the low cardiac output

Examination of the neck veins will usually show giant, presystolic auricular pulsations, due to the forceful contraction of the right auricle. A presystolic pulsation of the liver may also be present

The Heart.—The right ventricular hypertrophy may cause bulging of the precordium (Fig 38, page 153) and a strong systolic pulsation just to the left of the lower sternum. The obstruction to the flow of blood through the pulmonary artery produces a harsh systolic murmur, accompanied by

a systolic thrill, in the second and third left intercostal spaces, close to the sternum The murmur can be widely transmitted, even to the neck vessels

The pulmonary second sound may be soft or loud (In such a case, one is hearing a loud aortic second sound to the left of the sternum) A slight splitting of the pulmonary second sound may also occur. (This can occur normally and is due to asynchronism of the closure of the aortic and pulmonary valves) In spite of the physical signs of right ventricular hypertrophy, palpation of the pulmonary area will not show a systolic or a diastolic shock (which would indicate pulmonary hypertension)

Fluoroscopic and X-ray Examination.—Three characteristic signs are present: 1, enlargement of the right auricle and ventricle; 2, post-stenotic dilatation of the main pulmonary artery which shows weak pulsation; and 3, diminution of the pulmonary vascular markings

The post-stenotic dilatation of the main pulmonary artery may extend to the right, and occasionally to the left main branch of the artery. However, the remainder of the pulmonary vascular system is very inconspicuous. Therefore the lung fields are abnormally clear. Occasionally, the post-stenotic dilatation of the pulmonary artery resembles a pulmonary artery aneurism

Angiocardiographic Examination (L A O Position) (Fig. 91*C*, page 420).—The pulmonary valvular stenosis and the poststenotic dilatation of the pulmonary artery are well visualized

Catheterization Studies.—The pressure in the right ventricle is markedly elevated, and the pressure in the pulmonary artery is low, because of the pulmonary stenosis. Oxygen content values are normal. When the catheter is slowly withdrawn from the pulmonary artery, an abrupt rise in pressure occurs as soon as the stenotic valve is passed and the catheter tip enters the right ventricular cavity

Electrocardiogram.—Signs of right auricular hypertrophy and right ventricular hypertrophy are present A tall *P* wave will usually be seen in leads II, III, and *aVF*

Diagnosis.—The diagnosis of pulmonary valvular stenosis can be easily made on the basis of the following: large presystolic neck vein pulsation, systolic pulsation at lower left sternal border, a harsh systolic pulmonary murmur, accompanied by a systolic thrill, fluoroscopic findings of a large right ventricle, a large pulmonary artery which pulsates weakly, very clear lung fields, and electrocardiographic signs of right ventricular hypertrophy

An *auricular septal defect* may simulate pulmonary valvular stenosis. However, in an auricular septal defect, the pulmonary artery shows marked pulsations with a hilar dance, and the electrocardiogram usually shows right bundle branch block, rather than right ventricular hypertrophy In addition, the lung fields will be congested

An *Eisenmenger complex* may also simulate pulmonary valvular stenosis However, the dextroposition of the aorta can be seen on fluoroscopy in the *L.A.O.* position (page 415), the pulmonary artery pulsates widely, and the lung fields are markedly congested.

Congenital idiopathic dilatation of the pulmonary artery can also simulate pulmonary valvular stenosis, because in both conditions a systolic pul-

monary murmur and thrill may appear. However, in idiopathic dilatation of the pulmonary artery, physical signs, electrocardiogram, and x-ray findings show a normal right ventricle.

Catheterization studies of both conditions show a decreased pulmonary artery pressure. In idiopathic dilatation of the pulmonary artery, the drop in pressure in the pulmonary artery is due to dissipation of pressure as the blood flows into the dilated artery. However, the right ventricular pressure is also normal, in contrast to the right ventricular hypertension of pulmonary stenosis

Course and Prognosis.—Most patients with isolated pulmonary stenosis live to adulthood Death is usually due to right-sided heart failure or subacute bacterial endocarditis

Treatment—Pulmonary valvulectomy through the right ventricular wall (Brock's operation) is beneficial in those cases who show increasing dyspnea or heart failure, or progressive enlargement of the heart

Pulmonary Infundibular Stenosis.—In this second type of pulmonary stenosis, there is obstruction to the pulmonary blood flow in the outflow tract or infundibulum of the right ventricle, in the presence of a normal pulmonary valve The obstruction may consist of a diffuse narrowing of the infundibulum, or of a point of localized stenosis located in the outflow tract

Infundibular pulmonary stenosis is due to an arrest of the normal process of absorption and integration of the bulbus cordis into the right ventricle.

Clinical Picture.—The general picture of pulmonary infundibular stenosis is similar to pulmonary valvular stenosis, except in the following respects.

1. Large presystolic neck vein pulsations are usually not present.

2. The site of the maximal murmur and thrill are lower along the left sternal border than in pulmonary valvular stenosis, and may be noted best in the third or fourth interspace

3. The pulmonary artery is not dilated Hilar markings, however, are minimal, and the lung fields are abnormally clear, as in pulmonary valvular stenosis

4 When cardiac catheterization is done and the catheter is withdrawn slowly from the low pressure area of the pulmonary artery, an intermediate pressure zone may be found between the low pulmonary zone and the high right ventricular zone This intermediate zone is characterized by a low systolic pressure equal to the pulmonary artery systolic pressure, and low diastolic pressure, equal to the right ventricular diastolic pressure, in contrast to the higher diastolic pressure in the pulmonary artery.

Diagnosis—At the operating table, the following points can be used to differentiate pulmonary valvular from pulmonary infundibular stenosis In the valvular type, the systolic thrill can be felt close to the pulmonary valve, rather than over the right ventricular cavity, the sinuses of Valsalva are usually absent in pulmonary valvular stenosis and present in infundibular stenosis They can be seen externally as small, bluish, thin-walled areas on the vessel wall, just above the valve; in the valvular type, an infundibular chamber will not be visible externally

Treatment—Part of the infundibular tract can be removed surgically by using a special rongeur or cutting punch

Pulmonary Stenosis with a Patent Foramen Ovale.—Pulmonary stenosis (valvular or infundibular) may occur in association with a patent foramen ovale. So long as the right auricular pressure does not exceed the left auricular pressure, the foramen ovale will remain closed and the clinical picture will be that of an ordinary pulmonary stenosis. However, when the right auricular pressure exceeds the left auricular, venous blood will flow through the foramen ovale, producing a right-to-left venous-arterial shunt and cyanosis This may occur at birth, in early infancy, or may not occur until late in life

When the venous-arterial shunt occurs, the patients will show the usual physical signs of pulmonary stenosis. In addition, polycythemia, cyanosis and clubbing will appear

Diagnosis.—Pulmonary stenosis with a patent foramen ovale and a right-to-left shunt can be simulated by the tetralogy of Fallot. However, in the tetralogy, giant presystolic neck vein pulsations do not appear. In addition, the pulmonary artery area in the *P-A* view is concave, rather than convex, and a large pulmonary artery is not present. In addition, the heart is usually small in the tetralogy, unlike the large heart which occurs in pulmonary stenosis.

Angiocardiography is helpful in difficult cases, because in pulmonary stenosis, with a right-to-left shunt, immediate filling of the left auricle will be observed, whereas, the tetralogy will show instead early filling of the aorta

Treatment —Pulmonary valvulectomy is the treatment of choice.

Pulmonary Stenosis with an Auricular Septal Defect (Triad of Fallot).—Pulmonary stenosis (valvular or infundibular) can occur with an auricular septal defect, but with an intact ventricular septum When a left-to-right shunt is present, the clinical picture is that of pulmonary stenosis However, the patient may experience sudden, transient cyanosis on slight exertion. In addition, the hilar vessels may be more prominent than in an ordinary case of pulmonary stenosis

When a right-to-left shunt occurs through the auricular septal defect, the condition cannot be differentiated from pulmonary stenosis with a patent foramen ovale (see above)

The diagnosis is usually made as a result of cardiac catheterization or angiocardiography

Treatment —Although pulmonary valvulectomy has been done in this condition, there is evidence that when an auricular (or ventricular) septal defect is present, the operation should not be performed, because it may aggravate the left-to-right shunt by decreasing the pressure on the right side of the heart

Pulmonary Stenosis with a Ventricular Septal Defect.—Pulmonary stenosis (valvular or infundibular) can occur with an isolated ventricular septal defect This combination should not be confused with the tetralogy of Fallot, which includes dextroposition of the aorta.

The diagnosis of pulmonary stenosis with a ventricular septal defect is difficult and is usually made only by catheterization studies or angiocardiography. Since there is a left-to-right flow of blood through the septal defect, cyanosis and clubbing will be absent However, the electrocardiogram will show signs of right ventricular hypertrophy.

Treatment.—Pulmonary valvulectomy is contraindicated because if the right ventricular pressure decreases, the left-to-right shunt will increase and the right ventricular pressure will rise again to its preoperative level.

CONGENITAL ABNORMALITIES OF THE AORTIC VALVE REGION

Bicuspid Aortic Valve.—Abnormalities of the number of aortic valve cusps occur, and there may be two, four and even five cusps instead of three Two aortic cusps, bicuspid aortic valve, are the most common Similar congenital abnormalities may occur in the pulmonary valve However, most examples of bicuspid aortic valves are the result of acquired disease, usually rheumatic heart disease, and pathological differentiation of acquired from congenital bicuspid aortic valves may be very difficult

A bicuspid aortic valve produces no signs, but is frequently the seat of subacute bacterial endocarditis, and often occurs in association with coarctation of the aorta

Congenital Aortic and Subaortic Stenosis.—Subaortic stenosis is due to incomplete absorption of the bulbus cordis into the left ventricle, producing a band or membrane about 1 cm below the aortic valve The symptoms, signs and course and prognosis are the same as in acquired aortic stenosis There is no treatment

Differential diagnosis from acquired aortic stenosis may be impossible unless the characteristic basal systolic murmur has been present since infancy The murmur must also be differentiated from that of the Eisenmenger complex, page 356, and an isolated interventricular septal defect, page 354

Angiocardiography is occasionally helpful because it may reveal the subaortic stenosis In addition, it may show other abnormalities of the aorta, such as poststenotic dilatation, angulation of the isthmus, and even some degree of coarctation

Aortic valvulectomy can be done

Congenital Aortic Atresia —This is a rare condition usually associated with mitral atresia, hypoplasia or atresia of the ascending aorta to the point of insertion of the ductus arteriosus, and an underdeveloped or absent left ventricle Cyanosis is marked and death occurs in a few days. There is no treatment.

CONGENITAL ANEURISMS OF THE SINUSES OF VALSALVA

One or all of the sinuses of Valsalva, which lie just above the semilunar cusps of the aortic valve may be the site of aneurism formation (aortic root or sinus aneurism).

An aneurism of the right anterior sinus of Valsalva occurs most frequently. It extends downward, dissects the membranous portion of the interventricular septum and bulges into the cavities of the right and left ventricles

The left anterior sinus is the only one related to the external surface of the heart When a sinus develops in it, it produces a bulging into the pericardial sac to the left of the pulmonary artery. This aneurism also extends into the membranous portion of the interventricular septum.

An aneurism of the posterior (noncoronary) sinus of Valsalva also extends downward in the wall of the interventricular septum. It can bulge anteriorly into the left ventricle and posteriorly into right and left auricles.

These aneurisms of the sinuses of Valsalva may be congenital, or can be caused by syphilis, or bacterial endocarditis.

Symptoms and Signs.—So long as the aneurism does not rupture, it is usually symptomless However, it may compress the pulmonary or tricuspid valve and cause pulmonary or tricuspid stenosis It may distort the aortic valve and cause aortic insufficiency It may compress the superior vena cava, causing the superior vena caval syndrome It may press upon the interventricular septum and cause *a–v* block. Myocardial infarction has been reported as a result of compression of a coronary artery by the aneurism

Diagnosis.—If the aneurism is small, diagnosis may be impossible except by angiocardiography Here, a globular area of opacification will persist within the cavity of the left ventricle, after the dye is expelled from the left ventricle

A pericardial or mediastinal cyst can produce *x*-ray findings similar to those of an aneurism of a sinus of Valsalva Diagnosis can also be made by angiocardiography because the aneurism will be opacified and the other conditions will not

Course and Prognosis.—Depending on its anatomical location, the aneurism may rupture into the right auricle, right ventricle, left auricle, left ventricle, pericardium, mediastinum, pulmonary artery, superior vena cava or left pleural cavity

The clinical picture of rupture of an aneurism into the right ventricle or right auricle is similar to rupture of the interventricular septum (page 602). Rupture of an aneurism into the pulmonary artery is described on page 548, rupture into the superior vena cava is also described on page 548

At the time of rupture, the patient may experience severe substernal pain and dyspnea and may go into shock. A continuous, machinery type murmur develops over the upper sternum and signs of severe right-sided heart failure may rapidly develop. Death usually occurs in a few months. Signs of rupture may be present at birth, or may occur at any age.

Treatment.—There is no effective treatment

Congenital Aneurism of the Membranous Portion of the Ventricular Septum.—This can occur without an aneurism of a sinus of Valsalva It also can rupture into one of the cavities of the heart

TRICUSPID ATRESIA

Tricuspid atresia is associated with a hypoplastic right ventricle and a variety of other malformations However, *the following features are found* in all cases: 1, absence of the tricuspid valve; 2, auricular septal defect; 3, a large mitral orifice, and 4, hypoplasia of the right ventricle.

Other abnormalities which may or may not be present are: 5, a patent ductus arteriosus, 6, dextrocardia, 7, pulmonary stenosis (valvular or infundibular), 8, an absent or hypoplastic pulmonary artery; and 9, transposition of the great vessels

The presence or absence of transposition is important because it determines whether or not surgical treatment can be performed. Most of the cases are *not* associated with transposition and this type of tricuspid atresia will be described first.

Pathological Physiology.—The course of venous blood is therefore as follows. vena cava to right auricle, through the septal defect to left auricle and ventricle, to aorta and systemic circulation; and from the aorta through a patent ductus arteriosus to the lungs. Left ventricular hypertrophy occurs because the left ventricle must pump both venous and arterial blood

When a rudimentary right ventricle is present and the pulmonary artery is hypoplastic rather than atresic, a small interventricular septal defect may be present, so that the blood flows from the right auricle to the left auricle and ventricle. The blood then courses through the septal defect to *the right ventricle, pulmonary artery and the lungs. Other cases of tricuspid* atresia may be associated with transposition of the great vessels, the aorta arising from the rudimentary right ventricle, and the pulmonary artery from the left ventricle In such cases there is adequate circulation of the blood to the lungs

Symptoms.—These are the same as in the tetralogy of Fallot, page 418.

Signs.—Intense cyanosis and clubbing are usually present.

The Heart.—Because of the left ventricular hypertrophy, the apex may be as outside the left midclavicular line Murmurs are inconstant and may not be present The second sound at the base is clear and not reduplicated, because there is only one large vessel (the aorta) Since the flow of blood out of the right auricle is impeded because of the tricuspid atresia, the condition is similar to organic tricuspid stenosis, and the forceful auricular contraction may produce a presystolic pulsation of the liver. However, if the auricular septal defect is large, no liver pulsation occurs

Fluoroscopic and X-Ray Examination (Fig. 92).—Characteristic enlargement of the left ventricle is present·

P–A Position.—A concavity is present in the pulmonary artery segment region, giving the heart a contour similar to that of the tetralogy of Fallot. The hilar markings are minimal, and the lung fields are abnormally clear. Because the right auricle has difficulty in emptying its blood, the superior vena cava may be greatly dilated

R A.O Position.—No characteristic signs are present.

L A O. Position.—The large left ventricle bulges posteriorly into the shadow of the spine. Anteriorly, the absent or small right ventricle causes the cardiac shadow to run upward in almost a straight line to meet the aorta, leaving a very clear retrosternal space.

Because of the presence of a rudimentary right ventricle, the anterior border of the heart in the *L A.O.* position is composed of the right auricle. Therefore, an asynchronous pulsation of the anterior and posterior borders of the heart will occur in tricuspid atresia, the anterior border (the right auricle) contracting before the posterior border (the right ventricle).

TRICUSPID ATRESIA

P-A

LAO

RAO

Fig. 92.—Tricuspid atresia.

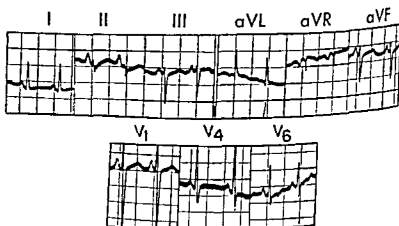


Fig. 93.—Tricuspid atresia. (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed., 1953.)

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Fluoroscopic and X-Ray Examination (Fig. 92) —Characteristic enlargement of the left ventricle is present:

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TRICUSPID ATRESIA

P-A

LAO

RAO

MLM

FIG. 92 — Tricuspid atresia.

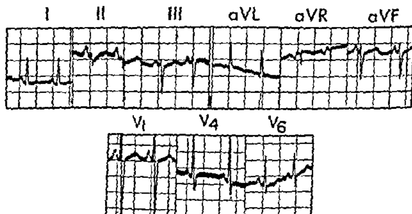


FIG. 93 — Tricuspid atresia. (*From* Goldberger, *Unipolar Lead Electrocardiography and Vectorcardiography*, Lea & Febiger, 3rd ed, 1953.)

Angiocardiographic Examination.—There is immediate entrance of the dye from the right auricle into the left auricle, left ventricle and the aorta. The pulmonary arteries and right ventricle are hypoplastic and their visualization is delayed.

Electrocardiogram (Fig. 93).—The large left ventricle produces a qR pattern with a tall R in lead aVL. Lead I also shows a qR and a tall R, and left axis deviation is present. Large P waves may also be present. The precordial leads show normal QRS complexes of the type seen in adults, and do not show tall R waves in leads $V_{1,2}$ which may occur in normal infants.

Diagnosis.—The presence of cyanosis and the electrocardiographic signs of a large left ventricle are almost pathognomonic, and the diagnosis can frequently be made on this alone. The x-ray findings are also very characteristic, although the backward bulging of the left ventricle in the L.A.O. position can sometimes occur in a case of congenital heart disease with a large right ventricle, where the apex is displaced backward.

Course and Prognosis.—Death usually occurs in a few months from heart failure or intercurrent infection. However, if the tricuspid atresia is associated with a functioning pulmonary artery and an interventricular septal defect, the circulation to the lungs may be sufficient to keep the child alive for several years, even if the ductus arteriosus closes.

Treatment.—In cases of tricuspid atresia with inadequate circulation to the lungs, the Blalock-Taussig operation is of value. The characteristics of the hilar markings and of the lung fields on x-ray examination give clues as to the adequacy of the pulmonary circulation.

Tricuspid Atresia with Transposition of the Aorta and the Pulmonary Artery.—In this type of tricuspid atresia, venous blood from the venæ cavæ enters the right auricle, passes through the auricular septal defect into the left auricle, then into the left ventricle, pulmonary artery and back again into the left auricle through the pulmonary veins. The only way that life can be maintained is either through a patent ductus arteriosus which pumps blood from the pulmonary artery into the aorta, or through a ventricular septal defect which allows oxygenated blood from the left ventricle to enter the rudimentary right ventricle and the aorta.

Clinical Picture.—Cyanosis is present, but it is not as intense as in cases of tricuspid atresia without transposition.

X-ray examination will show prominent hilar markings and mottled lung fields, indicating that a large quantity of blood is entering the lungs.

Angiocardiographic Examination.—There is early visualization of the left auricle, left ventricle and transposed pulmonary artery.

The Blalock-Taussig operation should not be done in these cases.

EBSTEIN'S ANOMALY OF THE TRICUSPID VALVE

The malformation in Ebstein's anomaly consists of fusion of the leaflets of the tricuspid valve into a membrane which extends downward into the right ventricle like a sheet or basket and divides the right ventricle into two portions—an upper auricular portion, and a lower ventricular portion. The valve leaflets may be completely fused with the endocardium of the

right ventricle so that the valve ceases to exist as such, and the orifice between the two portions of the right ventricle lies either between the free margin of the valve and the ventricular septum, or consists of an opening in the valve leaflet itself. The foramen ovale is usually patent. Rarely an auricular septal defect may be present.

Clinical Picture.—Because of the abnormal tricuspid valve, it is difficult for blood to pass from the right auricle into the right ventricle. As a result, the right auricle and the upper portion of the right ventricle dilate greatly. The right auricular pressure rises above the left auricular pressure, and since a patent foramen ovale is usually present, venous blood is shunted into the systemic circulation, causing chronic cyanosis. Since little blood enters the right ventricle, the flow of blood to the lungs is not adequate and dyspnea on exertion is a common complaint. A giant presystolic pulsation in the neck veins may be present, due to a forceful right auricular contraction.

Fluoroscopic and X-Ray Findings.—The heart has a globular shape, due to the greatly enlarged right auricle. The vascular pedicle at the base of the heart is narrow, and the silhouette resembles that of pericardial effusion. Hilar markings are not prominent, and the lung fields are abnormally clear.

Cardiac Catheterization.—It is often difficult to introduce the catheter into the right ventricle and the pulmonary artery because of the abnormal tricuspid valve. In addition, the catheter may coil and knot. Several deaths have occurred during catheterization in cases of Ebstein's anomaly.

Angiocardiographic Examination (P-A View).—Massive enlargement of the right auricle and the upper portion of the right ventricle are observed, as well as the abnormally low insertion of the tricuspid valve. There is a characteristic marked delay of several seconds before the dye is expelled from the right auricle. Then it passes quickly from the lower right ventricular chamber into the pulmonary artery, which is poorly visualized. (Because of this delay, the arm-to-lung circulation time is also prolonged.)

Electrocardiogram.—Right bundle branch block is a common finding. Signs of right auricular hypertrophy may also be present. Auricular arrhythmias frequently occur. A-V block may also occur.

Diagnosis.—Pulmonary stenosis with a patent foramen ovale (page 428) may produce a clinical picture very similar to Ebstein's anomaly. However, x-ray findings of a globular heart which resembles the picture of pericardial effusion, and right bundle branch block are suggestive of Ebstein's anomaly.

Treatment.—There is no effective treatment.

CONGENITAL MITRAL STENOSIS

This is a rare abnormality found in infants. It usually occurs in association with aortic stenosis, coarctation of the aorta or a *patent ductus arteriosus*. A defect of the auricular or ventricular septum is rarely present.

The diagnosis of congenital mitral stenosis is difficult. It can be suspected when an infant develops pulmonary edema, or when the clinical picture produced by other lesions, such as coarctation of the aorta, or a

patent ductus is atypical, or when the electrocardiogram shows right ventricular hypertrophy in the presence of a recognized left-sided lesion Cardiac catheterization may show an elevated pulmonary capillary pressure Angiocardiographic examination may show a characteristic delayed emptying of the left auricle.

ENDOCARDIAL FIBROSIS

Endocardial fibrosis (endocardial sclerosis, endocardial fibroelastosis, fetal endocarditis) is one of the most common non-cyanotic lesions causing enlargement of the heart in infants Anatomically, it consists of a yellowish-white thickening of the endocardium, particularly on the left side of the heart The left ventricle and left auricle may be involved and there may also be an associated deformity of the mitral and aortic valves. The process may also involve the endocardium of the right side of the heart. Scarring and fibrosis of the myocardium may also be present along with hypertrophy, especially of the left ventricle Occasionally, coarctation of the aorta of the adult type occurs in association with endocardial fibrosis

The cause of endocardial fibrosis is unknown Most investigators believe that it is a developmental defect One recent theory is that it may be due to anoxia, because it is often associated with other congenital malformations, which could produce endocardial anoxia. Such malformations include. 1, anomalous origin of the left coronary artery from the pulmonary artery This brings unoxygenated blood to the endocardium, 2, premature closure of the foramen ovale This would prevent oxygenated blood from entering the left auricle or ventricle; or 3, pulmonary or aortic valvular atresia, which can cause stagnation of blood in the chambers of the heart Other associated congenital abnormalities which may be present are hypoplasia of the aorta or even coarctation of the aorta of the adult type

Once the endocardial fibrosis develops, it can further damage the heart. It has been shown that a narrow zone of the ventricular subendocardial myocardium is nourished from blood contained within the ventricular cavities themselves Therefore when the endocardium becomes thickened and fibrosed, the orifices of the arterio-sinusoidal and arterio-luminal vessels which open into the endocardium may become obliterated, also causing subendocardial anoxia

Clinical Picture —Practically all cases occur during the first year of life The age at death usually ranges from birth to eight years However, some patients may recover and live to adulthood (Many, if not most cases of so-called idiopathic hypertrophy of the heart in adults may be due to a healed endocardial fibrosis) Most infants die between three and six months of age

Symptoms —Dyspnea and cough, due to left-sided heart failure, are the most common symptoms Other complaints include anorexia, vomiting, irritability, failure to gain weight or weight loss

Signs —Physical signs of an enlarged heart are usually present. However, murmurs are absent, or inconstant. Cyanosis is usually not present. When it does occur, it is often intermittent or terminal. Rales and enlargement of the liver may be present.

Electrocardiogram.—The most characteristic pattern is high voltage of the *QRS*, due to left ventricular hypertrophy, and/or signs of left ventricular strain Inasmuch as the position of the heart of an infant is usually vertical, the high voltage of the *QRS* will appear in leads II, III and *aVF*, in addition to the precordial leads from the left side of the chest (page 210)

X-Ray Examination—Signs of generalized cardiac enlargement are usually present

Diagnosis—Endocardial fibrosis can be simulated by the following:

Congenital malformations of the heart and great vessels, such as coarctation of the aorta, patent ductus arteriosus, aortic or subaortic stenosis, aortic-pulmonary septal defect, or tricuspid atresia A palpable femoral pulse practically excludes coarctation of the aorta. A patent ductus or aortic septal defect is unlikely in the absence of a loud murmur Tricuspid atresia shows electrocardiographic signs of left ventricular hypertrophy and strain, but marked cyanosis is also present.

Idiopathic Myocarditis (Fiedler's Myocarditis).—This may be due to a wide range of infectious agents, drugs, or to allergic sensitization, *etc.* (page 473) It occurs in infants and in children as well as in adults However, it is comparatively uncommon in babies under six months of age. The clinical picture is essentially that of right-sided heart failure, although left-sided heart failure can also occur

Idiopathic myocarditis can usually be differentiated from endocardial fibrosis because of the absence of electrocardiographic signs of left ventricular hypertrophy in myocarditis

Other conditions which can simulate endocardial fibrosis are von Gierke's glycogen storage disease (page 401), rhabdomyoma (page 402), anomalous origin of the left coronary artery from the pulmonary artery (page 402) and medial sclerosis of the coronary arteries (page 590)

MISCELLANEOUS CONGENITAL ENDOCARDIAL ABNORMALITIES

Chiari's network consists of fine fibers which lie in the right auricle, representing remnants of the right valve of the embryonic sinus venosus. Thrombi may form on the fibers and be the cause of pulmonary infarcts. Other anomalous bands and chordæ may be present in the auricles or ventricles Those in the ventricles may cause unusual musical murmurs.

CONGENITAL ABNORMALITIES OF THE VEINS

Complete Anomalous Pulmonary Venous Drainage.—Complete anomalous pulmonary venous drainage (transposition of the pulmonary veins, persistent left superior vena cava draining the pulmonary veins) is a rare condition, but can often be diagnosed during life. One or more of the pulmonary veins may empty into the right auricle, either directly, or into the coronary sinus of the right auricle, or into the right auricle by way of a persistent left superior vena cava or left innominate vein. The pulmonary veins may also drain into the ductus venosus, the portal vein, or the inferior vena cava.

If one pulmonary vein enters the right auricle, it does not cause any marked physiological disturbances However, if the entire pulmonary venous drainage is into the right auricle, marked dilatation of the right auricle and right ventricle and of the superior vena cava will occur, because the right heart receives not only all the venous blood, but all the oxygenated blood as well. Pulmonary congestion also occurs because of the large quantity of blood being pumped out of the right ventricle into the lungs.

The condition is compatible with life so long as the foramen ovale remains open, because it is through the foramen that blood reaches the left side of the heart and the systemic circulation



Fig 94 — Complete anomalous pulmonary venous drainage

Most patients with complete anomalous pulmonary venous drainage die within the first few months of life, or within the first year of life. However, if the foramen ovale is large, or if an auricular (or ventricular) septal *defect is present, the patient may live to adulthood*

Clinical Picture — Cyanosis is minimal in spite of the mixing of venous and arterial blood Physical signs of *right ventricular hypertrophy (page 425)* are present Murmurs are inconstant In some cases, a venous hum is heard between the fourth and second intercostal spaces, or higher, just to the left of the sternum.

Fluoroscopic and X-Ray Examination. — When all the pulmonary veins drain into the left superior vena cava, a characteristic x-ray picture occurs, if the infant lives more than a few months. The dilated vena cava is seen as a large, oval shadow in the *superior mediastinum*, *within which* the aortic knob and the shadow of the pulmonary artery can clearly be seen. The shadow is formed by the markedly dilated right and left superior

venæ cavæ and the left innominate vein. It forms a characteristic figure of 8 with the shadow of the heart (Fig. 94) The pulmonary hilar vessels may be engorged

Angiocardiographic Examination.—The abnormal entrance of the pulmonary veins into the right auricle can be visualized because the right auricle become reopacified at a time when the left heart is visualized.

Catheterization Studies.—When the oxygen content is raised in the superior vena cava, this indicates that the pulmonary veins are draining into the superior vena cava or into the left innominate vein. When the oxygen content of the *inferior vena cava* is high, this indicates that the pulmonary veins are draining into either the portal vein, the ductus venosus, or into the inferior vena cava itself If the oxygen content is raised only in the right auricle, this indicates that the pulmonary veins might be draining into the coronary sinus, or the right auricle directly.

However, other causes of a high oxygen content of the right auricle or the great veins include: an auricular septal defect, a systemic arteriovenous fistula, a ventricular septal defect with tricuspid insufficiency, or an aneurism of a sinus of Valsalva which has ruptured into the right auricle

Electrocardiogram.—Signs of right ventricular hypertrophy are present. In addition, a qR pattern is almost always present in lead V_1. This is, however, not pathognomonic of complete anomalous pulmonary venous drainage, and is merely due to the fact that extreme clockwise rotation of the heart is present.

Diagnosis—When the left superior vena cava is present, diagnosis can easily be made from the characteristic x-ray findings. However, in other cases, the clinical picture may simulate an auricular septal defect, (which may also be present in association with the anomalous pulmonary venous drainage) The presence of an RsR' pattern in lead V_1, and a completely normal arterial oxygen content would suggest the presence of an auricular septal defect rather than anomalous pulmonary venous drainage

Treatment—Theoretically, the condition can be cured by transplanting the left superior vena cava or the left innominate vein or one of the pulmonary veins into the left auricle Technically, this is a very difficult operation because the left auricle and the left auricular appendage are very small

Congenital Abnormalities of the Vena Cava.—The superior or the inferior vena cava or both may open into the left auricle instead of into the right auricle, causing underdevelopment of the right heart. This is a rare abnormality and can produce a clinical picture like tricuspid atresia. The diagnosis can be determined from angiocardiographic studies. Death occurs in a few months. Theoretically the condition can be cured by transplanting the abnormal vena cava into the right auricle. However, other abnormalities, such as dextrocardia, or levocardia with situs inversus, are always present.

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Chapter 27

ABNORMALITIES OF THE BRANCHIAL (AORTIC) ARCHES

THE development of the aorta and of the branchial arches was described on page 385. Abnormalities in the development of the branchial arches can produce the following conditions: right aortic arch, double aortic arch and other vascular rings around the esophagus and trachea, transposition of the aorta and pulmonary artery, persistent truncus arteriosus. These are described below. Congenital idiopathic dilatation of the pulmonary artery is also described in this Chapter, because it may be due to abnormal division of the truncus arteriosus into the aorta and pulmonary artery. Coarctation of the aorta is described in Chapter 28, page 453, and patent ductus arteriosus, in Chapter 29, page 464.

RIGHT AORTIC ARCH

Normally the arch of the aorta is formed by the fourth left branchial arch, and the pulmonary artery and the ductus arteriosus are formed from the sixth left branchial arch (page 387). However, if the fourth left arch fails to develop, the fourth right arch persists to form a right aortic arch. In such a case, the ascending aorta arises normally from the left ventricle, but the aortic knob arches to the right, compressing the esophagus on its right side instead of on the left. The aorta may continue its descent on the right side as a right descending thoracic aorta, swinging over to the left side just above the diaphragm (low crossing), or it may course over the right main bronchus, behind the trachea and esophagus, to form a normal left descending thoracic aorta (high crossing). The clinical picture and findings on fluoroscopic and x-ray examination depend on whether a right or left descending aorta is present.

Right Aortic Arch with a Right Descending Thoracic Aorta (Simple Right Aortic Arch).—A simple right aortic arch places no strain on the heart.

It may occur as an isolated abnormality. However, it occurs in about one-fourth the cases of tetralogy of Fallot, and can occur with other congenital abnormalities. Because of the presence of the right aortic arch, the innominate artery, which branches into the left subclavian and left common carotid arteries, is the first vessel to arise from the aorta; then the right common carotid and right subclavian arteries arise, all in mirror-image relation to normal (Fig. 96, *B*). In addition, the ligamentum arteriosum is also found on the right side, connecting the aorta to the right pulmonary artery.

Symptoms.—The condition is usually symptomless. However, stridor and hoarseness may occur, due to paralysis of the right vocal cord if a markedly dilated right aortic arch presses on the right recurrent laryngeal nerve as it passes beneath the arch.

Fluoroscopic and X-Ray Examination (Fig. 95) —The findings are pathognomonic.

P-A Position —The aortic knob is seen to the right of the sternum within the broad shadow of the superior vena cava which is pushed to the right by the ascending aorta. *The esophagus is compressed on its right side instead of on the left.*

If an *x*-ray film is taken with a Bucky grid and is overexposed, the trachea will also be seen deviated to the *left* in the region of the aortic arch.

RIGHT AORTIC ARCH WITH A RIGHT DESCENDING THORACIC AORTA

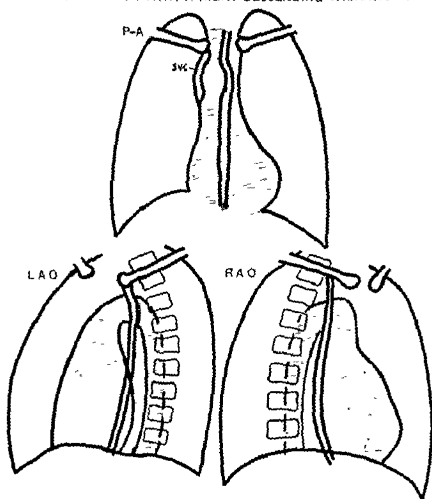


Fig. 95 —Right aortic arch with a right descending thoracic aorta. The cardiac configuration is that of the tetralogy of Fallot. SVC, Superior vena cava.

The shadow of the descending aorta will *not* be seen in its normal position along the left side of the vertebral column It may rarely be seen passing downward along the right side of the vertebral column. However, it will usually not be visible because it lies in front of the spine.

R.A.O. Position.—The aortic knob makes little impression on the esophagus or indents it from behind, producing slight forward displacement

L.A.O. Position.—The aortic knob indents the esophagus from the front, producing slight backward displacement.

Angiocardiographic Examination.—The right aortic arch is well visualized.

Course and Prognosis—The condition has no clinical significance unless it occurs with a tetralogy of Fallot or other condition amenable to the Blalock-Taussig operation, because in such cases, the operation is done on the side opposite to that in which the aorta arches (see page 394).

Right Aortic Arch With a Left Descending Thoracic Aorta (Retroesophageal Aorta).—In this condition, the aorta arches over to the right but almost immediately is pulled back to the left of the spine behind the esophagus, at the level of the bifurcation of the trachea (high crossing or retroesophageal aorta). This may occur in one of three ways:

1. The ductus arteriosus may develop normally from the left sixth arch instead of from the right sixth arch, pulling the aorta to the left as the ductus unites with the left pulmonary artery. In such a case, the ductus may be inserted into a diverticulum of the aorta situated at the junction of the right aortic arch with the descending aorta. The diverticulum is all that remains of the left aortic arch. The ductus in front, and the aorta behind the esophagus and trachea also produce a vascular ring (Fig. 96, *C*).

2. The left subclavian artery may arise from the aortic diverticulum to which the ligamentum arteriosum is attached, instead of from the innominate artery. Thus as the left subclavian artery courses up to the neck it pulls the dorsal aorta to the left (Fig 96, *D*).

3 A normal left aortic arch may be present in addition to the right aortic arch This produces a double aortic arch and a vascular ring around the trachea and esophagus (Fig. 96, *E*). The descending aorta in such a case lies to the left of the spine. The left arch in such cases is usually smaller than the right. Occasionally it may persist as a fibrous cord.

Symptoms—When a right aortic arch with high crossing, or a double aortic arch is present, symptoms, such as respiratory stridor, or dyspnea, due to pressure of the vessels on the esophagus and trachea may occur During early infancy, the stridor, which is mainly inspiratory, may be sufficient to cause cyanosis. Attacks of croup and pulmonary infections are also common, and a brassy cough may develop Solid food may be taken by the infant with difficulty, and vomiting may occur immediately after eating Since the right arch passes to the left side between the esophagus and the spine, it may erode the spine and cause intense pain later in life.

Signs.—The following signs have been described in adults: dullness on percussion along the right sternal border, extending up to the clavicle, visible systolic pulsation in the second or third right intercostal space; palpable strong systolic pulsation in the right supraclavicular fossa; maximum intensity of the aortic second sound above and to the right of its usual location—often it is heard best in the right supraclavicular fossa;

Occasionally symptoms are produced by a vascular ring associated with a right aortic arch and a right descending thoracic aorta. It is important to determine preoperatively whether the descending thoracic aorta lies on the right or left side, because the operation should be performed on the side on which the descending aorta lies.

An acute attack of dyspnea and cyanosis which occurs in an infant with a vascular ring can often be relieved by hyperextension of the head and neck.

OTHER VASCULAR RINGS COMPRESSING THE TRACHEA OR ESOPHAGUS

Aberrant Subclavian Artery.—Normally, the right subclavian artery arises from the innominate. Occasionally it arises from the distal part of

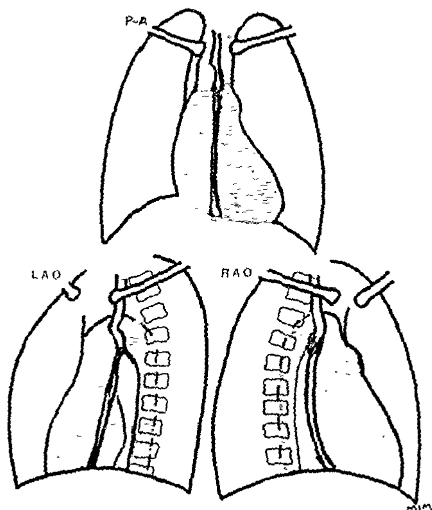


Fig. 97.—Right aortic arch with a left descending thoracic aorta

the aortic arch. As it ascends, it must deviate to the right to reach the right apex of the chest In doing so, it either runs behind the esophagus, or less commonly, it runs between the trachea and the esophagus. As a result, the infant may have difficulty in swallowing

An aberrant right subclavian artery can be easily diagnosed by *x*-ray examination of the barium-filled esophagus, because the pressure on the esophagus by the artery causes an oblique winding defect of the barium shadow in the *R A O.* position, and a posterior filling defect in the *lateral* position

If an aberrant right subclavian artery causes dysphagia, it can be ligated and divided.

Anomalous Innominate Artery.—If the innominate artery begins at a point farther to the left along the aortic arch than normal, it must wind around the anterior surface of the trachea as it runs upward and to the right to reach the right apex of the thorax. In this way it can compress the trachea and cause severe respiratory distress in an infant

Diagnosis can be made by *x*-ray examination. The esophagus is normal However, lipiodol studies of the trachea will show a compression of its anterior surface (A narrowing of the trachea can also be due to incomplete development of the tracheal cartilages In such a case, the caliber of the trachea will increase during inspiration and decrease during expiration)

An anomalous innominate artery can be corrected by pulling it forward and attaching it to the sternum so that it no longer touches the trachea

Anomalous Left Common Carotid Artery.—If the left common carotid artery begins more to the right than usual, it must wind around the anterior surface of the trachea to reach the left apex of the chest. In this way, it can cause respiratory distress in an infant

X-ray findings are similar to those which occur with an anomalous innominate artery. Treatment is also similar.

TRANSPOSITION OF THE AORTA AND PULMONARY ARTERY

In this condition, the aorta arises from the right ventricle, and the pulmonary artery arises from the left ventricle It is due to a failure of the bulbus cordis to undergo normal rotation (page 385). This failure of normal rotation is known as "detorsion"

Pathological Physiology.—Isolated transposition is not compatible with life because there would be no pathway for the interchange of unoxygenated and oxygenated blood Therefore there is always some other associated *abnormality present, such as a patent foramen ovale, a patent ductus* arteriosus, an auricular or ventricular septal defect, or a combination of these abnormalities Since venous blood is directed again to the systemic circulation, and oxygenated blood to the lungs, intense cyanosis usually occurs.

In the common condition of transposition with a patent ductus arteriosus and a patent foramen ovale, the flow of blood would be as follows: venous blood enters the right auricle and ventricle but is redirected to the systemic circulation through the aorta However, some oxygenated blood reaches

the descending aorta by way of the patent ductus arteriosus, the direction of the shunt being from pulmonary artery to descending aorta. Thus there is a tendency for the lower extremities to be slightly less cyanotic than the upper extremities. This zone of demarcation occurs at the brim of the pelvis. Some venous blood is able to reach the left side of the heart and the lungs for oxygenation by way of a patent foramen ovale.

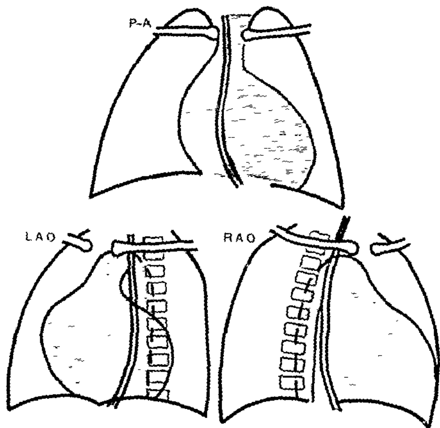


Fig. 98.—Transposition of the aorta and pulmonary artery.

Enlargement of both ventricles occurs. The right ventricle hypertrophies because it must propel blood through the systemic circulation. The *left* ventricle hypertrophies because it propels blood to both the descending aorta and to the lungs.

Signs.—Cyanosis and clubbing occur shortly after birth, the cyanosis being less marked below *the brim of the pelvis. The heart may* or may not be enlarged, and murmurs are inconstant.

Fluoroscopic and X-Ray Examination (Fig. 98).—The contour of the heart is often very characteristic:

P–A Position.—The vascular pedicle appears to be narrow. This is due to the fact that the transposed aorta lies almost directly in front of the pulmonary artery. A bulge may be present in the left mid-segment of the cardiac silhouette. This is due to the transposed ascending aorta. However, the region of the pulmonary artery may be concave. The lung fields are engorged, due to the increased volume of blood in the lungs. The cardiac shadow looks like an asymmetrical water-filled bag.

R.A.O. Position.—The pulmonary artery segment is small, but the right ventricle enlarged.

L.A.O. Position.—In this position the aorta and pulmonary artery lie side by side so that their shadow is much wider than in the *P–A* position. The large left ventricular shadow projects posteriorly beyond the spine.

Angiocardiographic Examination.—The transposed vessels can be visualized.

Electrocardiogram.—Signs of right ventricular hypertrophy are present.

Diagnosis.—Diagnosis is usually made from the x-ray findings and the association of pulmonary congestion with cyanosis. However, this can also occur in truncus arteriosus.

Course and Prognosis.—Death usually occurs early in infancy, though occasionally a patient will live through adolescence. Death is usually due to heart failure.

Treatment.—Surgical treatment is still experimental. Recently, an attempt has been made to correct transposition of the aorta and pulmonary artery by transposing all of the pulmonary veins and both venæ cavæ to match the abnormally reversed relationships of the aorta and the pulmonary artery.

PERSISTENT TRUNCUS ARTERIOSUS

The truncus arteriosus may persist instead of dividing into the aorta and pulmonary artery, as a result of the failure of the aortic and bulbar septa to develop (page 385). The truncus arteriosus is therefore always associated with a defect in the membranous portion of the interventricular septum. Other abnormalities may also be present. The pulmonary artery may arise from the truncus, or there may be pulmonary atresia. In such a case, the lungs are supplied by way of the bronchial arteries. Marked enlargement of both ventricles, especially the right, occurs as a result of the septal defect.

Signs.—Cyanosis may be minimal if a pulmonary artery is present, but is marked if there is pulmonary atresia. The heart shows signs of right ventricular hypertrophy, such as a systolic pulsation over the lower sternum and precordial bulging. A loud systolic murmur, associated with a thrill is usually heard over the upper sternum.

Dyspnea is common.

Fluoroscopic and X-Ray Examination (Fig. 99).—The cardiac silhouette is very characteristic and resembles a sitting duck.

P–A Position.—A large prominent aortic knob is present. The pulmonary artery segment is concave and the hilar markings minimal. The apex of the heart is high due to the large right ventricle.

the descending aorta by way of the patent ductus arteriosus, the direction of the shunt being from pulmonary artery to descending aorta. Thus *there is a tendency for the lower extremities to be slightly less cyanotic than* the upper extremities This zone of demarcation occurs at the brim of the pelvis. Some venous blood is able to reach the left side of the heart and the lungs for oxygenation by way of a patent foramen ovale.

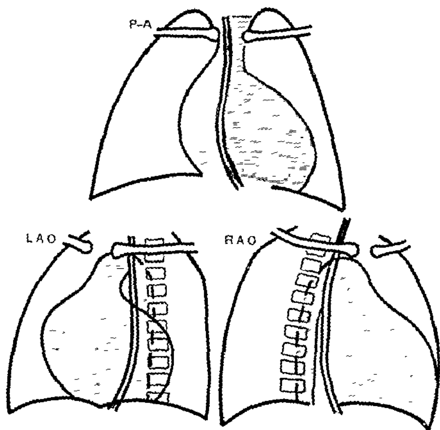


Fig. 98 —Transposition of the aorta and pulmonary artery

Enlargement of both ventricles occurs The right ventricle hypertrophies because it must propel blood through the systemic circulation. The left ventricle hypertrophies because it propels blood to both the descending aorta and to the lungs.

Signs—Cyanosis and clubbing occur shortly after birth, the cyanosis being less marked below the brim of the pelvis. The heart may or may not be enlarged, and murmurs are inconstant

Fluoroscopic and X-Ray Examination (Fig. 98).—*The contour of the heart is often very characteristic:*

Treatment.—In cases of truncus arteriosus with pulmonary atresia, the Blalock-Taussig operation is valuable. These cases show marked cyanosis in contradistinction to the cases of truncus arteriosus with a pulmonary artery.

CONGENITAL IDIOPATHIC DILATATION OF THE PULMONARY ARTERY

In this condition, there is simple dilatation of the pulmonary artery and its right and left primary branches, and absence of any other cardiac, arterial or pulmonary abnormalities which could otherwise produce the pulmonary dilatation There may be present an associated hypoplasia of the aorta.

Because of the dilated pulmonary artery, a loud pulmonary systolic murmur associated with a thrill may be present, and an accentuated pulmonary second sound X-ray examination and angiocardiography disclose the dilated pulmonary artery Catheterization studies are very characteristic because oxygen values are normal, the right ventricular pressure is normal, but the pulmonary artery pressure is lower than the right ventricular, due to dissipation of pressure as the blood flows into the dilated pulmonary artery (page 427)

Congenital idiopathic dilatation of the pulmonary artery is important because the physical and *x*-ray findings can simulate pulmonary stenosis, the Eisenmenger complex, a patent ductus arteriosus, *etc.* The diagnosis is made chiefly by exclusion, unless angiocardiographic and catheterization studies are done.

Cases of congenital idiopathic dilatation of the pulmonary artery have been reported in which cyanosis and right ventricular hypertrophy have been present. It is difficult to explain such findings on the basis of simple dilatation of the pulmonary artery.

CONGENITAL ABSENCE OF A MAIN BRANCH OF THE PULMONARY ARTERY

In rare cases, the right main branch, or the left main branch of the pulmonary artery is absent This condition can be diagnosed when a conventional *x*-ray film of the chest shows overdistention and mediastinal herniation of one lung, with hypoplasia and diminished vascularity of the affected lung. Diagnosis can be confirmed by angiocardiography. The condition does not cause severe respiratory symptoms.

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Chapter 28

COARCTATION OF THE AORTA

COARCTATION of the aorta consists of a localized or diffuse narrowing of the aorta at or distal to the insertion of the ligamentum arteriosum or the ductus arteriosus. It is customary to divide coarctation into two types, the adult type, and the infantile type The adult type is usually found in children and adults, whereas the infantile type is usually confined to infants, but occasionally the adult type of coarctation will be found in an infant, or the infantile type in an adult Coarctation of the aorta may also occur in unusual locations

Coarctation of the Aorta of the Adult Type.—In the adult type, there is a sharp zone of constriction, and sometimes even complete occlusion of the descending aorta, usually 1 cm or less in width, at or just below the point of insertion of the ligamentum arteriosum, rarely above (Fig. 100 ,A) Externally, the sharp constriction looks as if a ligature had been tied around the vessel.

The exact cause of the adult type is unknown The most likely explanation is that it represents a defect in the fusion of the left fourth and sixth aortic arches where they meet the dorsal aorta The theory that the adult type of coarctation represents an extension of the obliterative process that begins in the ductus is unsound because the coarcted area may be at some distance from the ductus, and in atypical cases may involve the aorta at the origin of the left subclavian artery The ductus arteriosus is always closed in cases of coarctation of the adult type, and only the ligamentum arteriosum remains

Pathological Physiology.—Because the constriction impedes the flow of blood to the lower extremities, several compensatory mechanisms appear

1 An extensive collateral circulation develops, principally by way of the left subclavian artery and its branches, especially the internal mammary arteries, the scapular artery and the intercostal arteries which become greatly dilated and tortuous. The intercostal arteries empty into the descending aorta, and the internal mammary arteries bring blood to the femoral arteries by way of the superior and inferior epigastric arteries

2. The increased resistance offered by the coarcted aorta causes hypertension of the upper part of the body, dilatation of the aorta proximal to the coarcted area, and left ventricular dilatation and hypertrophy. Poststenotic dilatation of the aorta distal to the point of coarctation may also appear This, however, is due to weakness of the aortic wall. (A similar poststenotic dilatation of the pulmonary artery occurs in cases of pulmonary stenosis and the tetralogy of Fallot.) Another mechanism can cause hypertension in cases of coarctation, namely renal ischemia, which results from the diminished blood supply to the kidneys (Goldblatt type kidney, page 557).

Coarctation may occur as an isolated abnormality. However, a congenital bicuspid aortic valve frequently is present. Occasionally subaortic stenosis with aortic insufficiency is also present. Abnormalities in other parts of the body, such as hypospadias, absent left kidney or horseshoe kidney, *etc.*, may appear. The most important of these is the presence of congenital aneurisms of the cerebral arteries.

Etiology.—The cause of coarctation is unknown. There may be some endocrine factor responsible for it, because it is much more common in males than females (4 or 5 to 1). Boys afflicted often show precocious physical development. Occasionally, however, puberty may be delayed Women with coarctation may show Turner's syndrome, namely: retarded growth, genital infantilism, pterygium colli (webbing of the neck), and cubitus valgus.

Symptoms.—*The patient is usually symptomless and the diagnosis is often made accidentally.* However, symptoms, such as headache, may

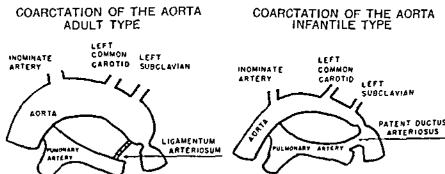


FIG 100 —*A*. Coarctation of the aorta of the adult type *B*, Coarctation of the aorta of the infantile type (After Burford and Carson)

appear due to the hypertension of the upper part of the body. Symptoms, such as coldness and numbness of the lower extremities, muscular weakness and intermittent claudication, due to the decreased circulation in the lower part of the body may also be present. Chest pain may occur, due to the large, pulsating collateral vessels, and transverse myelitis has even been produced by pressure on the spinal cord from a dilated anterior spinal artery.

Signs—The well-developed physical build of male patients has already been mentioned This is in contrast to the underdevelopment that may occur in patients with a patent ductus arteriosus or an interauricular septal defect. Cyanosis and clubbing are absent.

Blood Pressure and Pulse Findings.—Hypertension of the upper extremities is common, and the systolic pressure may exceed 200 mm. However, the systolic pressure may be within normal. More important than hypertension, however, is the finding that the systolic and usually the diastolic pressure in the lower extremities is lower than the pressure in the upper extremities. This is the reverse of normal (page 32)

In association with the decreased blood pressure in the lower extremities, the femoral artery and the other arteries of the lower extremity show weak or absent pulsations bilaterally. In addition, when the radial and femoral arteries are palpated simultaneously, the peak of the pulse wave will be felt to reach the radial artery before it reaches the femoral artery. This also is the reverse of normal (page 34).

Absent or weak pulsations in the abdominal aorta are present, in addition to the absent or weak pulsations in the femoral arteries Normally, the abdominal aorta bifurcates just below and to the left of the umbilicus Therefore, firm pressure with the fist should be made above the umbilicus in the epigastrium (The absence of abdominal aortic pulsations in an obese person has no significance.)

This sign can be used to differentiate coarctation of the aorta from thrombotic occlusion of the abdominal aorta (page 671), because in thrombotic occlusion of the aorta, femoral pulsations are weak or absent, but the abdominal aortic pulsations are strong

In cases where the coarctation involves the origin of the left subclavian artery, the blood pressure and pulse in the right radial artery is much greater than on the left side However, marked differences between the pulses and pressures of the right and left arms can occur normally (page 144)

In rare cases, the right subclavian artery may originate from the aorta below the obstruction. This causes the blood pressure in the right arm to be lower than in the left arm

Physical Signs of the Collateral Circulation—Pulsation of the dilated and tortuous superficial arteries can sometimes be seen over the back and scapular regions, especially if the patient bends forward slightly. Marked pulsations in the neck and suprasternal notch are also visible Murmurs and even thrills may be noted in the back and in the axillary region, due to the turbulent flow of blood in the dilated vessels, and a vascular murmur can even be traced down the sternum and over the abdomen along the course of the internal mammary and superior epigastric arteries

Coarctation of the adult type may also occur with a patent ductus arteriosus. In such a case, the cardiac findings are those of a patent ductus arteriosus. However, the femoral pulse and blood pressure are typical of the coarctation.

The Heart.—The heart may not be appreciably enlarged on physical examination but the aortic second sound is booming because of the hypertension An aortic systolic murmur of moderate intensity is usually present, transmitted to the neck and to the interscapular region, where it may be as loud as anteriorly This has been considered a very suggestive sign of coarctation The reason for this is that any loud murmur can be widely transmitted, but the farther from the source it is heard, the fainter it becomes Therefore, if the murmur of coarctation arises at the coarcted area, which is equally distant from the back and the anterior chest wall, it will be heard equally well in the back and the anterior chest wall. However, the murmur in the back may be produced locally by the dilated vessels as I pointed out above.

It has also been stated that a diastolic aortic murmur does not occur in uncomplicated coarctation of the aorta, and when present signifies an additional abnormality, such as a bicuspid aortic valve, subacute bacterial endocarditis of the aortic valve, or subaortic stenosis with aortic insufficiency. However, it has recently been demonstrated phonocardiographically that a diastolic murmur is usually present both over the precordium and over the back in cases of uncomplicated coarctation. The cause of the diastolic murmur may be a functional aortic insufficiency.

If subaortic stenosis and aortic insufficiency complicate a coarctation of the aorta, the diagnosis can be made because the systolic aortic murmur is harsh and rasping In addition, peripheral signs of aortic insufficiency, such as a collapsing pulse, *etc.*, are present in the upper extremities, whereas

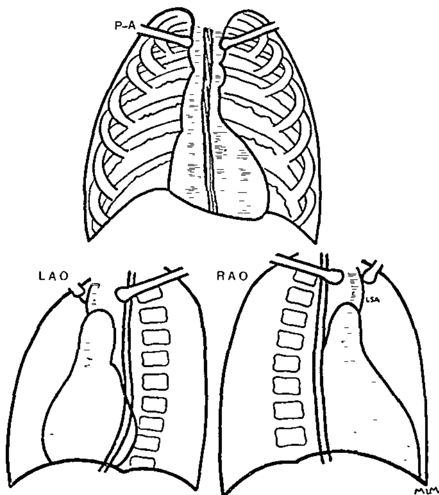


Fig. 101A —Coarctation of the aorta of the adult type Notching of the intercostal grooves of the ribs is also present. LSA, Dilated left subclavian artery.

in the lower extremities, pulsations are very poor, and Duroziez's sign (page 144) is not present.

Fluoroscopic and X-Ray Examination (Fig 101).—The following findings usually appear:

P–A Position.—The heart may or may not show left ventricular enlargement. The ascending aorta is dilated and even tortuous and may be visible to the right of the sternum However, the aortic knob is small and inconspicuous. A double knob is sometimes seen, the upper knob due to a large dilated pulsating left subclavian artery above a comparatively small aortic knob

Characteristic *x*-ray findings can be produced by a post-stenotic dilatation of the descending aorta which often occurs just below the site of the coarctation. In the *P–A* view, the shadow of this post-stenotic dilated

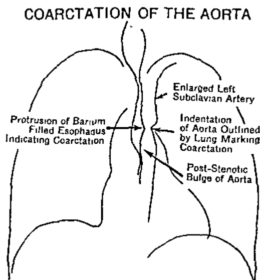


FIG 101*B* —Coarctation of the aorta (after Robbins and Wyman) See text for details

region may be superimposed on the shadow of the aortic arch, so that the arch appears to be lobulated just above the level of the left main pulmonary artery

This dilated area of the aorta may press upon the left side of the esophagus Esophageal compression also occurs from right intercostal arteries which cross the mediastinum to enter the distal aorta. This can produce the so-called "E-sign" in the barium-filled esophagus (Fig 101*B*).

Characteristic notching of the intercostal grooves of the third to the tenth ribs posteriorly may occur. This is due to erosion of bone by the dilated intercostal arteries Occasionally, notching of the superior border of the ribs occurs

Notching of the ribs rarely appears before the age of eight years. It is usually not seen until puberty, but it almost always is present in adults.

It has also been stated that a diastolic aortic murmur does not occur in uncomplicated coarctation of the aorta, and when present signifies an additional abnormality, such as a bicuspid aortic valve, subacute bacterial endocarditis of the aortic valve, or subaortic stenosis with aortic insufficiency However, it has recently been demonstrated phonocardiographically that a diastolic murmur is usually present both over the precordium and over the back in cases of uncomplicated coarctation. The cause of the diastolic murmur may be a functional aortic insufficiency.

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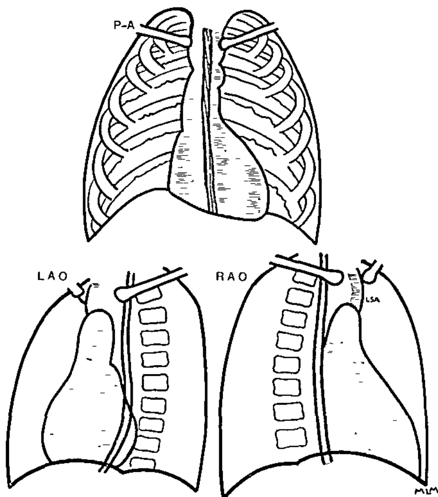


Fig. 101.1 —Coarctation of the aorta of the adult type Notching of the intercostal grooves of the ribs is also present LSA, Dilated left subclavian artery

In atypical coarctation involving the origin of the left subclavian artery, the left upper extremity may be colder than the right, and the patient may suffer from paresthesias on the left side. The left upper extremity may even be smaller than the right

Coarctation may be mistaken for essential hypertension in a young adult, or rheumatic heart disease with aortic stenosis because of the systolic aortic murmur The poor pulsations in the lower extremities can be mimicked by peripheral vascular disease with occlusion of one or more of the large arteries of the lower extremities, but in such cases, the process is usually unilateral In elderly patients bilateral absence of the femoral pulses can be produced by thrombosis of the abdominal aorta

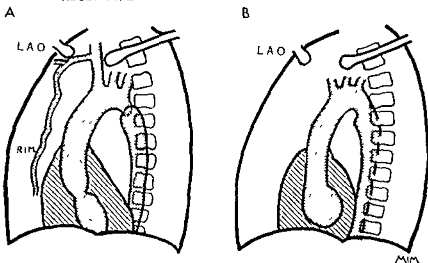


FIG 102 —*A*, Coarctation of the aorta Angiocardiogram in the L A O position RIM, Dilated right internal mammary artery
B, Patent ductus arteriosus Angiocardiogram in the L A O position

Course and Prognosis —About three-fourths of patients with the adult type of coarctation die before the age of forty years. Sudden death is not uncommon In most cases, death is due to one of the following conditions

1. *Rupture of the Aorta* —The point of rupture may be either in the ascending aorta, or in the descending aorta just distal to the coarctation. Instead of complete rupture, a dissecting aneurism of the aorta may develop, with signs due to the dissecting aneurism (page 660).

2 *Bacterial Endocarditis or Aortitis* —A bicuspid aortic valve, which is frequently present offers fertile ground for the implantation of bacteria. However, the endocarditis may develop on the mitral valve, and even on the wall of the aorta

3. *Heart Failure.*—Heart failure usually is the cause of death in patients who have associated cardiac lesions such as chronic rheumatic heart disease, coronary artery disease, *etc.*

4. *Subarachnoid Hemorrhage.*—This is usually due to rupture of a congenital aneurism of one of the arteries in the circle of Willis

5 Death, of course, can occur from incidental conditions

Infants with coarctation may develop very severe heart failure. They may appear healthy for days, or weeks, or months or longer, so long as the ductus arteriosus remains patent and blood can flow from the engorged aorta proximal to the coarcted region through the ductus into the lungs. When the ductus closes and this relief mechanism is lost, the left ventricle must pump blood into a vascular system which has a very high resistance because collateral channels have not yet formed. As a result, left-sided heart failure with dyspnea and cough occur. In addition, very severe right-sided heart failure may also develop.

Treatment.—The patient can be cured surgically by excision of the coarcted region and anastomosis of the proximal and distal ends of the aorta. In some cases, the segment of coarctation is so long that anastomosis is impossible In such cases, a human blood vessel graft can be used.

The best period for operation is between the ages of ten and twenty years Beyond the age of thirty or thirty-five years, the aorta becomes very atherosclerotic and difficult to suture.

When coarctation is discovered in an infant and if heart failure is not present, the operation should be deferred until the age of ten years. The reason for this is that the anastomotic site may not grow as well as the rest of the aorta, if the operation is done in infancy. If heart failure is present, this should be treated medically If the failure is persistent, operation on the infant may be life-saving.

Occasionally, postoperative weakness of the lower extremities with sensory changes and signs of pyramidal tract disturbances (anterior spinal artery syndrome) may occur This is due to injury to the anterior spinal artery during operation. However, the anterior spinal artery syndrome may occur in coarctation without operation, as a result of thrombosis of the artery

Another complication of the operation is the development of severe heart failure, due to the presence of associated valvular lesions, such as congenital mitral stenosis, or congenital aortic or subaortic stenosis.

Coarctation of the Aorta of the Infantile Type.—Coarctation of the aorta of the infantile type involves the isthmus of the aorta, the region from the origin of the left subclavian artery to the point of insertion of the ductus arteriosus (Fig 100, *B*). In some cases, the ascending aorta may also be involved, and in extreme cases, there may be absence of the aortic arch

The infantile type of coarctation is due to faulty development of the fourth left branchial arch. It always occurs in association with a patent ductus arteriosus, and often with other abnormalities, such as severe septal defects, transposition of the aorta and pulmonary artery, *etc.*, which usually cause death in early infancy. However, patients with an uncomplicated type of infantile coarctation may live to adult life

Pathological Physiology.—The collateral circulation which is seen in the adult type of coarctation does not develop in the infantile type Arterial blood to the head and upper extremities is carried by way of the ascending aorta. However, the lower extremities receive venous blood which passes from the pulmonary artery through the ductus to the descending aorta. As a result, cyanosis may develop in the lower extremities. In infants, the zone between the acyanotic and cyanotic regions is at the brim of the pelvis (Another cause of cyanosis of the lower extremities is a patent ductus arteriosus with pulmonary hypertension—page 468)

Signs—The infantile type of coarctation rarely occurs as an isolated abnormality and diagnosis is difficult. In patients who reach childhood or adult life, the physical signs are predominantly those of the patent ductus arteriosus which is present. In addition, there are absent or feeble pulsations in the lower extremities, and often some degree of cyanosis. Rarely, a patent ductus arteriosus may be present with the adult type of coarctation.

Course and Prognosis.—This depends on the associated cardiac abnormalities

Treatment—There is no treatment.

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Chapter 29

PATENT DUCTUS ARTERIOSUS

During fetal life the lungs do not function, and most of the blood from the pulmonary artery is directed to the aorta through the ductus arteriosus (ductus Botalli), thus short-circuiting the lungs. At birth or shortly thereafter, the ductus ceases to function, but it may be two months and in some cases six months and even seven to fourteen years before complete obliteration occurs. A strand, the ligamentum arteriosum, may remain, or all signs of the ductus may completely disappear.

The ductus arteriosus may persist after birth under two sets of conditions:

1 As an isolated abnormality Here it serves to embarrass the circulation in a way described below. In such a case, surgical interruption of the ductus will be beneficial and even lifesaving.

2 In association with other congenital abnormalities, such as tricuspid atresia, or absence of the aortic arch, *etc.*, where the ductus acts as the major blood vessel bringing blood to the lungs for oxygenation. In such cases severance or spontaneous closure of the ductus will result in death of the patient

Pathological Physiology.—A patent ductus actually is an arteriovenous fistula (the pulmonary artery carries venous blood) and produces many of the signs of a peripheral arteriovenous fistula (see page 664). During systole, as much as 20 to 75 per cent of the blood pumped by the left ventricle into the aorta passes back through the ductus into the pulmonary artery. This greatly increases the work of the left ventricle whose cardiac output must increase proportionately to the amount of blood shunted, to supply the needs of the body. During diastole, the blood continues to flow through the ductus from the aorta to the pulmonary artery, causing the diastolic blood pressure to fall. In addition, the blood shunted into the pulmonary artery may raise the pressure in the pulmonary circulation and increase the pressure against which the right ventricle must work, putting a strain on the right ventricle However, the pulmonary circuit has a passive resistance to a large degree, so that even with an increased blood flow, dilatation of the pulmonary vessels occurs without an increase in pulmonary pressure. Thus, it has been found that in the usual case of patent ductus arteriosus, the right ventricular and pulmonary artery pressures are normal.

Since the flow of blood is always from the aorta to the pulmonary artery, cyanosis does not occur. Theoretically, venous blood could flow from the pulmonary artery to the aorta, causing cyanosis, but clinically it does not occur, unless independent pulmonary pathology occurs, producing pulmonary hypertension.

The size of the ductus may vary greatly It is usually between 0 5 and 0.7 cm. in diameter. Occasionally aneurismal dilatation may occur Its average length is from 0 7 to 1 cm., but it may be so short that the aorta and pulmonary artery lie in apposition with each other Arteriosclerotic changes may occur in the ductus with plaque formation and calcification, and in rare cases, spontaneous thrombosis of the ductus may occur

Etiology —Recent studies have indicated that spontaneous closure of the ductus at birth is stimulated by the rise in oxygen content of the blood Thus, obstruction to the air passages in a newborn baby may hinder closure of the ductus. However, it is possible that the ductus may lack some normal inherent tendency to undergo obliteration

Symptoms.—There are no symptoms of a patent ductus arteriosus unless the patient becomes conscious of the loud murmur, or of pounding of the heart

Signs —Examination may reveal the following signs If the amount of blood shunted through the ductus is excessive, an inadequate amount is available for the systemic circulation and stunting of growth may occur, causing the patient to have a frail, gracile appearance This, however, is not a constant sign Cyanosis and clubbing are characteristically absent

A patent ductus is much more common in females than in males

Blood Pressure Studies —The systolic blood pressure is usually normal, the diastolic pressure low, producing an increased pulse pressure When this is marked, peripheral signs suggestive of aortic insufficiency, such as capillary pulsation (page 140), Duroziez's sign (page 144) *etc* , may occur. Average blood pressure values are systolic, 100 to 125 mm , diastolic, 45 to 60 mm.

The following test has been suggested to diagnose patent ductus arteriosus: A control blood pressure reading with the cuff on the left arm, is taken with the patient standing The patient exercises by taking 10 knee bends or their equivalent The blood pressure is taken immediately thereafter

Normally, or in conditions such as an auricular septal defect which can simulate a ductus arteriosus, the diastolic pressure falls less than 10 mm on exercise In patent ductus, the diastolic pressure falls more than 15 mm and the actual level of the diastolic pressure may reach 20 mm Hg or even 0 mm However, a similar fall in diastolic pressure occurs after exercise in aortic insufficiency, hyperthyroidism, in febrile patients and in any case with peripheral vasodilation

The Heart and Blood Vessels —The neck vessels may be dilated and pulsating. Marked pulsation may also be noted in the first, second, and third left intercostal spaces, below the clavicle

A characteristic, almost pathognomonic continuous murmur is present in the first, second and third intercostal spaces to the left of the sternum This murmur has been variously described as having the roar of running machinery, of a train in a tunnel, or of a humming top The murmur is almost always harsh and loud, rarely blowing. A peculiarity often observed is that it appears to become louder during the latter part of systole, enveloping the second sound, and then continuing with decreasing intensity during diastole.

The systolic component is transmitted over the precordium to the neck, even to the back. The diastolic component is usually not transmitted so widely and is best heard over the left side of the chest. The systolic component is due to the rush of blood from the aorta to the pulmonary artery during systole The diastolic component is due to the continued flow of blood from the aorta to the pulmonary artery even during diastole. However, it may be due in part to functional pulmonary insufficiency. The murmur is best heard on lying, becoming fainter on standing. The pulmonary second sound is accentuated.

Even in infants and young children, the typical, continuous, machinery murmur is usually present by the age of eighteen months. However, in infants under one year of age, a systolic murmur alone is common. The absence of the continuous murmur in infants is due to the relatively high pressure in the pulmonary circulation compared to the systemic circulation. This allows blood to flow rapidly through the ductus only during systole.

The continuous murmur may also be absent in children if pulmonary hypertension is present (see page 468)

At the apex, a systolic murmur is usually present. Sometimes an apical mid-diastolic murmur appears, *different in characteristics from the diastolic* component of the continuous murmur The apical diastolic murmur may be due to the rapid flow of blood from the left auricle into the left ventricle during early diastole (see Functional Mitral Stenosis, page 168)

Fluoroscopic and X-Ray Examination —A prominent pulmonary artery is usually seen with dilated and forceful pulsating hilar vessels, resulting in a "hilar dance" (page 193). There may be signs of slight or moderate left ventricular enlargement Frequently, the heart is normal in size. Rarely, there is generalized cardiac enlargement Since the ductus pulls the pulmonary artery upward, *the aortic window (page 61) may be obliterated in* the L A O position. The left auricle may appear moderately enlarged in the R A.O position Mild to moderate congestion of the lung fields, especially in the right lower lobe, has been reported

Angiocardiographic Examination (L.A O. Position) (Fig. 102*B*) —A characteristic but not pathognomonic localized dilatation of the descending aorta anteriorly at the level of the ductus is usually seen Only rarely is the ductus opacified

In some cases, a characteristic defect in the outline of the main pulmonary artery *can be seen two to three seconds after the injection of the* contrast medium The defect is due to blood which does not contain the contrast medium, flowing from the aorta through the ductus to the pulmonary artery

Catheterization Studies —Catheterization studies are valuable because the oxygen content of the pulmonary artery is significantly greater than that of the right ventricle (see page 223).

In some cases, a characteristic pulse pressure may be obtained by continuous recording of the pressure while the catheter is slowly withdrawn *from the right pulmonary artery into the right ventricle.* The change consists of an abrupt rise in the systolic and diastolic pressures at the site of the ductus. This is accompanied by a change in the pulse contour. One explanation for these local changes is that they represent the transmission of the systemic pressure through the patent ductus.

Electrocardiogram.—The tracing usually remains normal. However, signs of left ventricular strain or hypertrophy may appear in rare cases

Diagnosis—The presence of a machinery murmur in the second left intercostal space, absence of cyanosis (slight clubbing may occur if the patient has developed subacute bacterial endocarditis), a wide pulse pressure, a prominent pulmonary artery on *x*-ray examination, a normal electrocardiogram, and a history of a murmur since childhood are practically pathognomonic of a patent ductus arteriosus.

A machinery murmur in the second left intercostal space can occur after a rupture of an aortic aneurism into the pulmonary artery, or a rupture of an aneurism of the sinus of Valsalva, or of an aortic root aneurismin to the right auricle or ventricle. However, in such cases, there is a sudden onset of pain, intense dyspnea and signs of severe right-sided heart failure In rare cases, the clinical picture of a patent ductus arteriosus may be simulated by a congenital fistulous communication between the aorta and pulmonary artery (aortic-pulmonary fistula) (page 470). A machinery murmur may also occur in the tetralogy of Fallot, due to dilated bronchial arteries beneath the sternum

Patients with aortic insufficiency may also show a double murmur to the left of the sternum, but the murmur is not continuous, and there are usually signs of marked left ventricular hypertrophy Similarly patients with an interauricular septum defect, or an Eisenmenger complex may have a double murmur in the pulmonary area, but in such cases physical, electrocardiographic and *x*-ray signs of marked right ventricular hypertrophy are present A patent ductus arteriosus in association with other congenital lesions may also produce the characteristic machinery murmur However, in such cases, cyanosis and clubbing are often present, or signs of the associated congenital abnormality

If a patent ductus arteriosus produces only a systolic murmur, there is no way except by angiocardiographic or catheterization studies to establish the diagnosis

Course and Prognosis—If left untreated, about 70 per cent of patients with an isolated patent ductus arteriosus will die before the age of forty years. Common causes of death are heart failure and bacterial endocarditis Rupture of the dilated pulmonary artery rarely is a cause of death. Another rare complication is paradoxical embolism from the mitral or aortic valves or the left auricle or ventricle to the lungs by way of the ductus

Subacute bacterial endocarditis usually develops at the pulmonary side of the ductus where the abnormal current strikes against the vessel wall Occasionally the endocarditis arises at the aortic side. Emboli are carried to the lungs, and signs of pulmonary infarction appear early, splenic infarcts and petechiæ later That is why it may be difficult to get a positive blood culture at first

Aneurismal dilatation of the ductus may occur if the ductus becomes obliterated at the pulmonary side, but not at the aortic side. When this happens, the physical and laboratory signs are those of an aneurism, not of a patent ductus. Rarely the aneurism ruptures, causing death Another rare complication is aneurism of the pulmonary artery, either proximal or distal to the ductus.

Treatment —The only treatment for a patent ductus arteriosus is to surgically divided or ligate the ductus. Indications for operation are (a) stunting of growth; (b) development of heart failure; (c) development of bacterial endocarditis.

In patients with bacterial endocarditis, the operation can be done as soon as possible because ligation of the ductus can cause healing of the endocarditis. However, some cardiologists believe that it is preferable to treat the endocarditis with antibiotics and defer operation on the patient for several months until the inflammatory reaction in the ductus subsides. This is a preferable course, because the infected ductus may be very friable

An associated simple interventricular or interauricular defect with a left-to-right shunt is not a contraindication to surgical closure of an open ductus Such cases will not show cyanosis or decreased arterial oxygen saturation Similarly, a ductus arteriosus associated with pulmonary stenosis and closed septa, can also be treated surgically. At a later date, the pulmonary stenosis can also be corrected, if necessary.

In general, operation should not be undertaken before the age of four years, because spontaneous closure or marked reduction in size may occur up to that age Similarly, if the diagnosis is first made in a patient over thirty years who is symptomless, operation can be deferred indefinitely because the development of subacute bacterial endocarditis or heart failure is then slight. Some cardiologists believe that all patients with an isolated patent ductus arteriosus should have surgical treatment. However, the surgical mortality even with an experienced surgeon is not negligible, though it should be under 10 per cent The best age for operation is at about five to six years

After a successful operation, the machinery murmur should disappear. In some cases, a systolic pulmonary murmur may persist months after the operation When the ductus is ligated and not severed, recanalization may occur with the redevelopment of a machinery murmur. In other cases a double murmur may persist, due to coincident rheumatic or congenital involvement of the aortic valves.

A contraindication to operation is the presence of cyanosis and clubbing, because in such cases the patent ductus may be necessary for life.

ISOLATED PATENT DUCTUS ARTERIOSUS WITH A *RIGHT-TO-LEFT SHUNT (REVERSE DUCTUS)*

If pulmonary hypertension occurs in a case of isolated patent ductus arteriosus, the pulmonary artery pressure may become greater than the pressure in the aorta, and the blood may flow through the ductus from the pulmonary artery to the aorta, rather than in the more usual way.

The cause of the pulmonary hypertension in such cases is obscure. It may be due to one of four factors: 1, It may be the result of multiple, small pulmonary emboli occurring over a long period of time. This is probably the most satisfactory explanation. 2, It may be a late complication of the usual patent ductus arteriosus, namely, to the prolonged increase in total pulmonary blood flow. 3, It may be due to an antecedent

pulmonary arteritis with partial thrombosis of one or more branches of the pulmonary artery. 4, It may be due to the persistence of the high pulmonary vascular resistance which is normal in the fetus.

Clinical Picture.—The symptoms and physical signs depend on the degree of pulmonary hypertension and the degree of the right-to-left shunt.

Patent Ductus Arteriosus with Transient Right-to-Left Shunt.—When pulmonary hypertension is present, but the pulmonary artery pressure is not higher than the aortic pressure, a right-to-left shunt will occur, for example, only after strenuous exercise, or after some unusual occurrence, such as labor.

Symptoms are minimal The patient may complain of dyspnea on exertion.

Physical signs are not characteristic of a patent ductus arteriosus. There is no machinery murmur. Instead, a harsh, pulmonary systolic murmur, or a harsh, pulmonary systolic and a blowing pulmonary diastolic murmur are present The pulmonary second sound is accentuated and may be split Cyanosis and clubbing are absent.

Electrocardiogram will show either right ventricular strain or hypertrophy.

Fluoroscopic and x-ray examination will show a large, actively pulsating pulmonary artery, with moderate enlargement of the right ventricle

The diagnosis can be confirmed only by cardiac catheterization studies and by simultaneous brachial and femoral arterial oxygen determinations

Cardiac catheterization shows pulmonary hypertension and no signs of an intracardiac shunt The pulmonary artery will show a higher oxygen content than the right ventricle, just like the usual case of a patent ductus

Simultaneous arterial oxygen determinations of the brachial and femoral arteries may show that the femoral arterial blood has an oxygen content significantly lower than that of the brachial artery, especially after exercise

Treatment —Surgical ligation of the ductus is advisable in these cases

Patent Ductus Arteriosus with Permanent Right-to-Left Shunt.—When the pulmonary hypertension occurs early in infancy or childhood, the pressure in the pulmonary artery becomes higher than the aortic pressure The result is that there is a more or less constant entrance of pulmonary unoxygenated blood into the descending aorta

The ductus enters the descending aorta beyond the origin of the great vessels from the arch Therefore, venous blood flows primarily to the *lower extremities* *As a result, the femoral arterial oxygen* content is significantly lower than the arterial oxygen content of the upper extremities Cyanosis therefore occurs early in infancy or childhood and often shows a very characteristic distribution, being greater in the lower extremities than in the arms or hands (see page 125). In addition, clubbing may be more marked in the toes than in the fingers.

Symptoms may include dyspnea on exertion, cough or hemoptysis, easy fatigability, and "a feeling as if my legs are going to fold up under me," due to the passage of unoxygenated blood into the descending aorta and femoral arteries. Anginal pain on exertion may also occur.

Physical signs, fluoroscopic, *x*-ray and catheterization findings are similar to cases where the shunt is only transient (see above). Because of the mixing of venous and arterial blood, polycythemia and an elevated hematocrit value occur with the cyanosis.

Treatment.—Ligation of the ductus must *not* be done in cases where cyanosis is present, because the ductus acts as an escape valve and reduces the work of the right ventricle If the ductus is ligated in such a case, the patient may die from acute right-sided heart failure.

AORTIC-PULMONARY SEPTAL DEFECT

An aortic-pulmonary septal defect (aorticopulmonary septal defect, aortic septal defect, partial persistent truncus arteriosus, aortic-pulmonary fistula) is a relatively uncommon defect and consists of a windowlike opening, usually 10 to 12 mm. in diameter, between the aorta and the pulmonary artery, usually immediately above the valves. The semilunar valves of both vessels are normal and the cardiac septa are closed. The condition is due to a partial deficiency of the primitive aortic septum which divides the embryonic truncus arteriosus into the ascending aorta and the main pulmonary artery

The clinical picture of an aortic-pulmonary septal defect is identical with that of a patent ductus arteriosus, including the occurrence of a continuous, machinery-like murmur at the base of the heart.

Differential diagnosis between an aortic-pulmonary septal defect and a patent ductus arteriosus is very difficult The continuous murmur of an aortic-pulmonary septal defect may be heard loudest nearer the sternum than the continuous murmur of a patent ductus

On fluoroscopic examination in the *L.A O.* position, an aortic-pulmonary septal defect will show marked *pulsation of the ascending aorta*, whereas in patent ductus arteriosus, it is the aortic arch which pulsates markedly.

On catheterization of the heart, the catheter will tend to go up to the arch of the aorta in an aortic-pulmonary septal defect, whereas, in patent ductus arteriosus when the catheter enters the aorta from the pulmonary artery, it tends to go downward

At the operating table, it is possible to differentiate between the two conditions In a patent ductus arteriosus, a thrill can be felt in the pulmonary artery, opposite the distal end of the aortic arch, and digital pressure over the ductus abolishes the thrill In an aortic-pulmonary septal defect, the thrill is most intense in the first part of the pulmonary artery, just above the pulmonary valve and within the pericardial sac. Digital pressure in this region is necessary to stop the thrill (A similar thrill can occur with an Eisenmenger complex with associated aortic insufficiency.)

Retrograde aortography in the *L.A.O.* position may show the dye entering the pulmonary artery from the aorta just above the semilunar valves, before the arch of the aorta is opacified.

Surgical correction of an aortic-pulmonary septal defect has been done, but the operation is often very difficult because the fistulous communication between the two vessels is usually too short to ligate.

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Chapter 30

MYOCARDITIS

The clinical diagnosis, myocarditis, fell into disrepute in the early part of the century, following a period in which the term had been used indiscriminately to designate any cardiac disorder not accompanied by abnormal murmurs As a result, many conditions were incorrectly diagnosed as myocarditis, and for many years the myocardial fibrosis resulting from myocardial infarction was incorrectly designated as "chronic myocarditis" Later, many pathologists refused to make a diagnosis of myocarditis except in cases of rheumatic fever or diphtheria However, myocarditis is a recognized entity

Pathology.—There may be focal circumscribed areas of inflammation involving chiefly the interstitial tissues (interstitial myocarditis) with infiltration of histiocytes, lymphocytes and of polymorphonuclear leucocytes between the muscle fibers and in the perivascular connective tissue In other cases, there is predominantly necrosis of the muscle fibers (parenchymatous myocarditis). In most cases, there is evidence of both interstitial and parenchymatous involvement

Etiology.—The following classification of myocarditis can be used

1 **Specific Myocarditis**—In such cases the heart shows a characteristic anatomic structure or identifiable pathologic organisms, as in rheumatic fever, tuberculosis, blastomycosis, *etc.*

2 **Myocarditis Following Infectious Diseases**—There may or may not be an associated endocarditis or pericarditis

3 **Myocarditis Due to Chemical Poisons, Physical Agents, or Hypersensitive States.**

4 **Acute Isolated Myocarditis (Fiedler's Myocarditis).**—This is a form of myocarditis not associated with any known illness It is essentially an interstitial myocarditis with infiltration of polymorphonuclear and eosinophilic leucocytes, lymphocytes, plasma cells and endothelial cells Most cases occur in young adult males, but it may affect all age groups There is evidence that some cases of isolated myocarditis are the result of hypersensitivity of the heart to sulfonamides or other substances

5 **Myocarditis of Unknown Etiology.**

Some of the more common conditions in which the various types of myocarditis have been found are the following. diphtheria, rheumatic fever, subacute bacterial endocarditis, scarlet fever, pneumonia, rickettsial diseases, meningococcemia, Weil's disease, relapsing fever, syphilis, South American trypanosomiasis (Chagas' disease), schistosomiasis, malaria, trichinosis, acute encephalitis, poliomyelitis, infectious mononucleosis, measles, infectious polyneuritis (Guillain-Barre syndrome), mumps, infectious hepatitis, smallpox, virus pneumonia, tuberculosis, sarcoidosis, coccidiomycosis,

blastomycosis, actinomycosis, torulosis, septicemia, acute glomerulonephritis, acute tonsillitis and nasopharyngitis, cellulitis, lymphangitis and wound infections, tularemia, brucellosis, exfoliative dermatitis, arsenical reactions, sulfonamide hypersensitivity, starvation, heat stroke, carbon monoxide poisoning, burns, emetine, *etc.* Interestingly enough, myocarditis is not usually found in typhoid fever or in bacterial dysentery.

Symptoms and Signs.—The clinical picture of myocarditis is usually obscured by the primary disease process, and myocarditis, when present, is usually overlooked. There may be a disproportion between pulse and temperature Ordinarily, the pulse should rise eight to ten beats for each degree rise in temperature, whereas in myocarditis, the pulse may be inordinately high This does not always occur. There may be hypotension, with the systolic pressure below 90 mm , and a thready and feeble pulse. The patient may complain of weakness, substernal oppression and dyspnea, and cyanosis and orthopnea may be present. A diastolic gallop may appear, or embryocardia with a tic-toc rhythm, and signs of right-sided or left-sided heart failure

Fluoroscopic and X-Ray Examination.—Moderate or marked generalized enlargement of the heart may be present, and the cardiac silhouette appears hazy. the sharp outline of the various chambers having disappeared.

Electrocardiogram.—The electrocardiographic changes are for the most part nonspecific There may be changes in the *T* wave, *RS–T* segment, *Q–T* interval, *P–R* interval, and premature contractions, paroxysmal tachycardia, nodal rhythm, *a–v* block and *a–v* dissociation, auricular fibrillation or auricular flutter may appear. However, any or all these abnormalities may occur when myocarditis is absent. The only electrocardiographic sign that I consider significant is the presence of *RS–T* deviations such as occur in pericarditis. In other words, I do not believe that a diagnosis of myocarditis can be made from the electrocardiogram in the light of our present knowledge

***Course and Prognosis.**—This is difficult to evaluate. It depends on the* etiology of the myocarditis However, sudden death may occur fróm myocarditis even during the course of an innocuous disease, such as an upper respiratory infection. It is also probable that many of the cases of cardiac hypertrophy of unknown etiology are the result of healed myocarditis

Some of the more important types of myocarditis are considered below:

Diphtheria.—The exotoxin of the Klebs-Loffler bacillus is the cause of the diphtheritic myocarditis. The more important cardiac lesions consist of degeneration and necrosis of the muscle cells. In addition an interstitial myocarditis is present Involvement of the endocardium or pericardium is rare

The cardiovascular complications of diphtheria take place usually at about the beginning of the second week of the disease. The clinical picture is often that of shock, although heart failure may occur with a gallop rhythm or embryocardia The development of a slow pulse indicates that *a–v* block has occurred. Splitting of the heart sounds may appear if bundle branch occurs.

Electrocardiogram.— *RS–T* deviations, *T* wave changes and a prolonged *Q–T* interval often appear. In addition, various grades of *a–v* block, from

a prolonged P–R interval to complete a–v block may appear Intraventricular conduction disturbance or bundle branch block may also develop. Other abnormalities which may appear are nodal rhythm, a–v dissociation, auricular flutter or fibrillation or paroxysmal tachycardia.

Course and Prognosis.—Diphtheritic myocarditis is a serious complication of diphtheria, especially when more advanced degrees of a–v block or intraventricular conduction disturbances or bundle branch block develop, and these signs often are a forerunner of death However, if the patient recovers, the arrhythmias and abnormal electrocardiographic patterns usually revert to normal

Treatment—The diphtheria should be energetically treated with antitoxin Heart failure is treated in the ordinary way Shock can be treated with the pressor drugs (page 284)

Rheumatic Fever.—See Chapter 31, page 481

Scarlet Fever.—It is my opinion that the carditis of scarlet fever is identical with that of acute rheumatic fever (page 484) However, if suppurative complications, such as a purulent otitis media, osteomyelitis, *etc*, occur, a resulting septicemia may cause a bacterial endocarditis and a purulent carditis with myocardial abscesses

Pneumonia.—Pneumonia may cause myocarditis However, heart failure is an unusual complication of pneumonia unless preexisting heart disease is present In such cases, heart failure is precipitated by the increased work of the heart resulting from the fever, cough, retention of sodium which occurs in pneumonia, and from an increased pulmonary resistance in the consolidated lung

The blood pressure usually remains unchanged, but may fall in a hypertensive patient, due to the nonspecific effects of fever and bed rest. If shock develops, the fall is precipitous and associated with other signs of shock.

The diagnosis of left-sided heart failure complicating pneumonia is difficult It may be suggested if a rise in the pulse rate and an increase in dyspnea or orthopnea not related to a rise in temperature occur The recognition of shock offers no difficulty.

Fluoroscopic and X-Ray Examination—Moderate enlargement of the heart has been reported during pneumonia However, the enlargement may be more apparent than real, and may be due to elevation and splinting of the diaphragm

Electrocardiogram.—Nonspecific T wave changes and RS–T deviations may occur. RS–T deviations characteristic of myocardial injury may appear if pericarditis develops

Laboratory Tests—The venous pressure remains normal, unless right-sided heart failure or pericardial effusion with tamponade develops. The arm-to-tongue circulation time usually remains normal, but prolongation has been reported in the absence of myocarditis, especially in the older age groups.

Course and Prognosis—The occurrence of heart failure or shock during pneumonia is serious, but the patient may recover.

Treatment—The pneumonia should be vigorously treated with appropriate antibiotics The prophylactic use of digitalis in patients with pneu-

monia is not indicated. If shock occurs, pressor drugs (page 284) should be used. It may also be necessary to treat the coëxisting dehydration with intravenous glucose and distilled water, or with plasma.

Tuberculosis.—Tuberculous myocarditis is very rare in contrast to tuberculous pericarditis. It may occur from direct extension of the pericarditis, or during the course of acute miliary tuberculosis. Tubercles or tumor-like nodules (tuberculoma) are found. In some cases, a large, solitary tubercle or cold abscess occurs. Heart failure may result, or *a–v* block (if the conduction system is involved), and even an aneurism of the heart with rupture The myocarditis may extend to the endocardium, causing a tuberculous endocarditis. However, isolated tuberculous endocarditis may also occur in rare cases

The diagnosis of tuberculous myocarditis is difficult, and symptoms and signs are obscured by the clinical picture of tuberculosis elsewhere in the body The occurrence of *a–v* block or sudden unexplained heart failure in a patient with tuberculosis may suggest myocardial involvement. However, one should remember that chronic rheumatic heart disease, or hypertensive heart disease, or coronary artery disease, is not too infrequent in patients with pulmonary tuberculosis, but is often disregarded. In addition, chronic pulmonary tuberculosis may produce cor pulmonale and heart failure without any direct tuberculous involvement of the heart (Chapter 40, page 626) *RS–T* deviations in the electrocardiogram suggestive of myocardial injury are usually due to a tuberculous pericarditis rather than to myocarditis.

The treatment is that of the general tuberculous process.

Sarcoidosis.—The heart is occasionally involved in sarcoidosis. Non-caseating tubercle-like infiltrations occur. The myocarditis is usually symptomless, but heart failure and *a–v* block have been reported as a result of sarcoid myocarditis However, symptoms, such as dyspnea, may result from the pulmonary lesions of sarcoidosis.

Trichinosis.—Although it is rare for trichinella larvæ to be found in the heart at autopsy, pathological evidence of myocarditis is not uncommon. The electrocardiogram may show *RS–T* deviations, such as occur with pericarditis In spite of the myocardial involvement, symptoms and signs referable to the heart are uncommon.

Poliomyelitis.—The cardiovascular abnormalities which occur during the acute phase of poliomyelitis may include myocarditis, hypertension, electrocardiographic abnormalities, pulmonary edema and shock

The myocarditis is characterized by necrosis of the heart muscle cells and by a neutrophilic infiltration. A focal, interstitial infiltration of lymphocytes also occurs, but this can occur in the hearts of patients dying of even non-infectious diseases

Two types of hypertension have been described The first type is probably related to hypoventilation and anoxia, and can be eliminated by the use of oxygen, or by respirators, *etc* The second type of hypertension seems to be related to injury of the hypothalamus and may persist long after the patient recovers from the poliomyelitis. A malignant type of hypertension may develop, with eye ground changes, hypertensive encephalopathy, or pulmonary edema.

The electrocardiographic changes which appear are nonspecific. The P–R interval may be prolonged In addition, the T may be flattened or reversed, the Q–T prolonged and RS–T deviations may appear These changes are most often due to the hypopotassemia which is frequently present (page 206)

In practically all cases of fatal bulbar poliomyelitis, the terminal event is shock.

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Chapter 31

RHEUMATIC FEVER

RHEUMATIC fever is responsible for about 95 per cent of heart disease in childhood, and for more than one-third of the cases of heart disease observed in adults; and during the first two decades of life it causes more deaths than all the communicable diseases together

PATHOLOGY

The fundamental lesion of rheumatic fever consists of fibrinoid swelling of the ground substance of the connective tissue, followed by an infiltration of inflammatory cells, which may or may not form the characteristic lesion of rheumatic fever, namely the Aschoff body, depending on the tissues affected

Rheumatic Myocarditis —The characteristic lesion of rheumatic activity in the myocardium is the Aschoff body This is preceded by a localized fibrinoid swelling of the ground substance of the connective tissue The collagen fibrils become swollen and some fragmentation of the fibrils may occur Then, in about ten to fourteen days, this area of fibrinoid swelling is surrounded by characteristic large Aschoff cells. These cells have a granular, basophilic cytoplasm, large vesicular nuclei, frequently multiple, with a dense membrane, and with centrally placed, stellate, hyperchromatic nucleoli. The grouping of the cells often occurs in the form of a fan or rosette, or palisade A few polymorphonucleated leucocytes, lymphocytes, plasma cells and an occasional eosinophile may be present This collection of cells surrounding an area of swollen or fragmented collagen is known as an Aschoff body or nodule It is characteristically found around blood vessels or in the interstitial tissues, and is small and submiliary in size Larger Aschoff bodies occur when two or more small bodies coalesce Over a period of time, the Aschoff cells elongate and assume the appearance of fibroblasts, the inflammatory reaction becomes less marked, until finally, a small microscopic scar may be the only evidence of previous rheumatic activity.

The Aschoff bodies may be found anywhere in the myocardium, especially in the interventricular septum, the wall of the left ventricle and the left papillary muscles, the right ventricle, and occasionally in the auricles.

Rheumatic Valvulitis.—On the valves, small, gray-pink verrucæ are seen especially along the lines of closure of the leaflets, most commonly on the mitral and aortic valves, infrequently on the tricuspid valve, and rarely on the pulmonary valve. The verrucæ can also occur on the chordæ tendineæ Microscopically, the verrucæ are composed of granular and acidophilic material protruding from the leaflet, and uncovered by endothelium. The larger verrucæ may show a fibrin covering. In the substance of the valve beneath the verrucæ, typical Aschoff bodies may occur, or there may be

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the typical pathological changes of rheumatic activity are not observed because the brain substance has little connective tissue Subcutaneous nodules probably represent collections of Aschoff-like bodies.

ETIOLOGY

Rheumatic Fever as an Allergic Response to Streptococci.—Although the exact mechanism of rheumatic fever is unknown, much evidence has accumulated that rheumatic fever in some way is related to antecedent streptococcal infections, and that the pathological findings of rheumatic fever constitute an allergic response of the heart and other tissues of the body to one or more streptococcal products Before discussing these relations, a few words might be said about streptococci in general:

Streptococci were formerly described according to their effect on red blood cells when grown on blood-agar plates Thus, streptococci which produced slight hemolysis of red cells with some greening were called alpha streptococci, or streptococci viridans. Streptococci which produced frank hemolysis were known as beta hemolytic streptococci. Gamma streptococci produced no hemolysis or greening of red cells. This classification has been superseded for the most part by the newer methods of studying the antigenic properties of the streptococci and their products For example, it has been found that streptococci (pathogenic and non-pathogenic) elaborate a specific carbohydrate, which enables most streptococci to be divided into groups A, B, C, D, *etc.* With but few exceptions, all the streptococci pathogenic for man belong to group A. (Classification of the streptococci viridans into groups has proven difficult, although some strains have been found to belong in group D)

Group A streptococci, which includes the old beta hemolytic class, can be further divided into more than forty types, depending on the presence of type-specific proteins, which are labeled M and T

The streptococci of group A can elaborate one or more of the following substances

1 Streptokinase (fibrinolysin) which has the capacity to dissolve a blood fibrin clot. Antibodies to streptokinase are formed in the body during the course of a streptococcus infection, and can be quantitatively studied

2 Hemolysins, or streptolysins, which dissolve red blood cells and release hemoglobin to the surrounding medium Two types of streptolysins are produced, streptolysin O, which is oxygen labile, and streptolysin S, which is extractable only in the presence of serum Because of technical difficulties, the antibodies formed only to streptolysin O are studied clinically These antibodies are called antistreptolysin O

There is some evidence that streptolysin S may play a role in the pathogenesis of rheumatic fever The serum of most people contains protective substances against streptolysin S The concentration of these protective substances is related to the serum phospholipid level. When the serum inhibitor of streptolysin is low, the serum phospholipid level is low. Phospholipid contains choline, which the human body can neither synthesize nor store in significant amounts. Eggs constitute the richest dietary source of choline. And it has been found that children who have had repeated

attacks of rheumatic fever either had a deficient egg intake or a low phospholipid blood level.

3. Other substances produced by group A streptococci are a proteolytic enzyme, known as streptococcus proteinase, and hyaluronic acid and hyaluronidase The streptococci responsible for scarlet fever also produce an erythrogenic toxin.

The Relation of Hyaluronic Acid and Hyaluronidase to Rheumatic Fever.—Recent studies indicate that disturbances involving hyaluronic acid or hyaluronidase may be related in some way to the rheumatic infection

Hyaluronic acid is a mucopolysaccharide which exists in the skin as well as in the ground substance of the connective tissue, *etc.*, and is influential in protecting the skin and connective tissue from bacterial invasion. It probably is produced by young connective tissue cells. The enzyme, hyaluronidase, which is specific for hyaluronic acid can be produced by some strains of group A streptococci. Hyaluronidase promotes bacterial invasion by depolymerizing hyaluronic acid and allowing substances (toxins, *etc.*) to spread through the connective tissue. This effect of hyaluronidase, which is known as the spreading factor, can be inhibited by salicylates Hyaluronidase also causes the sedimentation rate to become more rapid, *in vivo and in vitro*

The links between hyaluronidase and rheumatic fever are the following: Since the basic lesions of rheumatic fever are essentially in connective tissue, the possibility that an enzyme, such as hyaluronidase, elaborated by streptococci may produce injury to the ground substance of the connective tissue has been considered; and it has been noted that patients with rheumatic fever develop a significant anti-hyaluronidase titer in their sera; and that there is a good correlation between the anti-hyaluronidase titer and the activity of the rheumatic process. However, the streptococcic infections which precede rheumatic fever are caused by those types of group A streptococci which produce hyaluronic acid and not hyaluronidase. In addition, there have been no reported instances in which rheumatic fever followed an infection with either type 4 or type 22 group A streptococci, the two types which produce hyaluronidase instead of hyaluronic acid. Thus, the mechanism by which the anti-hyaluronidase titers develop in patients with rheumatic fever is still unknown

The relationship of rheumatic fever to streptococci can be seen from the fact that an attack of rheumatic fever is usually if not invariably preceded by an infection due to group A streptococci (tonsillitis, otitis media, scarlet fever, *etc.*). In addition, during the course of acute rheumatic fever, there is usually a sharp rise in antistreptolysin O titer, and in antifibrinolysin titer in the blood

The allergic basis of rheumatic fever rests upon observations that after the initial streptococcus infection, there is a latent period of one to four weeks, averaging about two weeks, at which time the typical picture of rheumatic fever appears. The latent period is similar to that which precedes the allergic condition of serum sickness. In addition, Klinge, Rich, and others have been able to reproduce the pathological changes of rheumatic fever, including the Aschoff bodies, by allergic sensitization of animals.

The streptococcal product which acts as the antigen producing rheumatic fever is not known. In this connection, it has also been postulated that even if streptococcal products are not antigenic, their conjugation with human proteins in the blood stream may give rise to substances which are antigenic.

Heredity and Constitutional Factors.—Some evidence has been adduced that the susceptibility to rheumatic fever is inherited as a single recessive character. Thus, if both parents are positive, that is, have a history of rheumatic fever, according to this theory, the chances that their children will develop rheumatic fever are practically 100 per cent If one parent is positive, while the other has merely a positive father or mother, chances that a given child will develop it are 50-50 If neither parent is positive, but each has a positive parent, the chances are 1 to 4 However, epidemiological studies of the incidence of rheumatic fever during epidemics tend to cast doubt on these relations. There is, nevertheless, a high familial incidence of rheumatic fever

Children with rheumatic fever do not have any typical body build, but freckled and red-headed children seem to be more prone to rheumatic fever than other children.

Regional and Seasonal Aspects of Rheumatic Fever.—Rheumatic fever is much less prevalent in the Southern and Pacific States than in the Middle Atlantic States, and when attacks do occur in warm climates, they are usually mild. Attacks of rheumatic fever are also more common in winter and spring than in other times of the year. These facts have an important bearing on the treatment of convalescence and prophylaxis, and it has been found that sending a child to Florida or any warm climate from November to April, or instituting prophylactic therapy during these months may be very valuable in warding off recurrences (*also see* page 491)

Social and Economic Factors.—Although rheumatic fever occurs among well-to-do children, poverty, malnutrition, unhygienic and cold, damp surroundings greatly increase its incidence

Racial Differences.—No race is immune from rheumatic fever In the United States, the mortality of colored children is higher than of white children This may be related to the lower economic status of the colored children

Age—Rheumatic fever may occur at any age group, even in the elderly, but it rarely begins below the age of three and after twenty-five. The first attack usually begins between the ages of four and fifteen years, and especially between the ages of five and nine

SYMPTOMS AND SIGNS

Rheumatic fever is usually divided into the following four phases:

Phase 1, the phase of invasion, consisting of an upper respiratory infection due to a group A streptococcus

Phase 2, the latent or asymptomatic phase, which may vary in length from a few days to several weeks

Phase 3, the phase of activity, with the onset of rheumatic manifestations This phase may last an indefinite time

Phase 4, the inactive phase, when signs of rheumatic activity have finally disappeared

The clinical picture of rheumatic activity may vary from an attack so mild that the child is not even put to bed, to acute fulminating cases which result in death in a few weeks. It is not at all rare in taking a history of a patient with chronic rheumatic valvular disease, to be told that the patient never had rheumatic fever, but that during childhood there was a period of tiredness and easy fatigability, some shortness of breath after play, or loss of appetite, loss of weight or failure to gain weight, frequent nose bleeds, vague abdominal pains or vague muscular or arthralgic pains especially in the calves or the heels, which the parent dismissed as "growing pains" Occasionally the story of a persistent low-grade fever after tonsillitis is obtained These neglected symptoms, in reality manifestations of rheumatic activity were the direct cause of the patient's valvular heart disease. However, a typical attack of rheumatic fever usually includes some symptoms and signs of polyarthritis or carditis

Acute Rheumatic Polyarthritis.—With an acute attack of polyarthritis or arthralgia, there is a sudden rise in temperature even to 104° or more and severe prostration The large joints are usually involved, especially the ankles, knees and elbows. Symmetrical joints are often simultaneously affected Monoarticular arthritis is most uncommon. The joints are reddened, hot, tender to palpation, and painful on motion. There is effusion into the joint, and in addition, the periarticular tissues are swollen. The synovial exudate is turbid due to marked numbers of polymorphonuclear leucocytes, but the fluid is sterile

Inflammation of a joint lasts from four to six days, if no therapy is given, and as the inflammation begins to subside, the arthritis spreads from one set of joints to another, the fever rising as each new set of joints is involved. In about ten to fourteen days, the fever ebbs and disappears and no further joint manifestations appear. This sequence is known as the monocyclic form of polyarthritis in contrast to the polycyclic form where the inflammation reappears in joints that had been previously inflamed a few days previously, and in contrast to the continuous form of polyarthritis where signs of joint inflammation may persist for weeks However, one of the characteristic features of rheumatic polyarthritis is the prompt response of the arthritis and the fever to salicylates.

Acute Rheumatic Carditis.—*Every fatal case of acute rheumatic fever* shows signs of carditis at autopsy, and clinical signs of carditis can be detected in more than half the cases of acute rheumatic fever that recover. In mild cases, there may be practically no evidence of carditis except for the presence of a tachycardia out of proportion to the fever. For example, with a temperature of 101°, the pulse may be 140 or more. (The pulse ordinarily rises 8 or 10 beats for each degree rise in temperature.) In addition, the pulse rate remains elevated during sleep. In more severe cases, generalized dilatation of the heart occurs. This may give rise to murmurs and signs of congestive heart failure. A soft, blowing apical systolic murmur usually appears, due to the cardiac dilatation.

In addition, an apical diastolic and even a presystolic murmur may be present. This is also due to cardiac dilatation and is not a sign of mitral stenosis, which takes several years after an attack of rheumatic fever, to

develop. Proof of this is the disappearance of the murmur as the rheumatic activity subsides A pulmonary systolic murmur also may be present, but this has no significance. The intensity of the murmurs vary from day to day The intensity of the first heart sound at the apex also shows daily variations in intensity (page 158). A tic-tac quality to the heart beat may also appear. Gallop rhythm may be present, but in children this has no significance unless signs of congestive heart failure are present. When heart failure appears, it is predominantly right-sided, and the liver may extend to the level of the umbilicus or below it Râles in the chest and edema are late signs. An irregular rhythm, due to incomplete *a–v* block, or *a–v* dissociation with interference or auricular fibrillation, or even premature contractions may be present.

Fluoroscopic and *x*-ray examination will confirm the enlargement of the heart. Not only is the size of the heart enlarged, but the sharp delineation of the cardiac borders is replaced by a hazy outline. When cardiac dilatation occurs in the presence of a heart previously enlarged because of chronic rheumatic heart disease, the roentgenologic appearance may simulate pericarditis with massive effusion, and pericardial taps are often done on such patients, in the erroneous belief that fluid is present.

However, pericarditis, either serofibrinous or with effusion, may occur even though there may be no or few clinical signs of pericarditis present. Occasionally a characteristic to-and-fro friction rub appears The rub may persist even if much fluid accumulates Usually there is less than 300 cc of fluid, but more than a liter may form.

Other Manifestations of Rheumatic Fever.—Low-grade Fever.—If the child is kept at bedrest, the temperature, taken 4 times daily, at 8 A M , noon, 4 P M and 8 P M., will fluctuate more than 1 5° in the absence of overt signs of infection, such as tonsillitis, sinusitis, *etc* However, an oral reading of slightly above 99° or a rectal temperature slightly above 100° is not necessarily abnormal In addition, even marked fluctuations in temperature can occur in the absence of rheumatic fever, as in cases of neurocirculatory asthenia (page 311)

Acute Chorea.—When the rheumatic process affects the brain, the clinical picture of acute chorea (St Vitus's dance, Sydenham's chorea) results Chorea may be the first manifestation of rheumatic activity It usually occurs between the ages of ten and fourteen years, especially in girls It rarely occurs in infants Pregnancy favors its development or reappearance. The onset is usually gradual and is characterized by involuntary but conscious muscular jerks and twitches, which are rapid and of fairly wide excursion and resemble a gesticulation or a grimace The movements usually stop during sleep Ataxias also are present and result in a stumbling gait, mumbling speech, overreaching on pointing tests, and some loss of muscular power. There is usually dulling of perception and diminished ability to concentrate. Signs of pyramidal tract involvement with a positive Babinski reflex, also occur.

These symptoms are usually accompanied by a slight fever. Polyarthritis, subcutaneous nodules and signs of carditis may also be present.

Most cases of chorea last from ten to twelve weeks, but the duration may be as long as six months. Recurrences are common. Death is unusual and when it does occur is usually due to an associated carditis.

Other Neurological Manifestations of Rheumatic Fever.—Occasionally acute rheumatic fever is ushered in by headache, nuchal rigidity and meningismus with a positive Kernig sign, or with high fever and delirium, mental confusion, convulsions, or coma, the clinical picture resembling an acute infection of the central nervous system, rather than rheumatic fever. However, spinal tap reveals normal findings. Occasionally, the arthralgia of rheumatic fever may cause so much muscle splinting that the muscular weakness of poliomyelitis is simulated

Subcutaneous Nodules.—These are almost pathognomonic of rheumatic fever, but also occur in rheumatoid arthritis. They are described on page 118

Pleuritis, with or without effusion, and occasionally a rheumatic pneumonitis, with signs of consolidation, may occur. Various skin manifestations may appear, especially the marginate type of erythema multiforme (erythema marginata) This is characterized by a rash which begins as flat papules which rapidly increase in size, even in the course of a few hours, at the same time clearing in the center, and fusing with one another, so as to produce an irregular circular ring of erythema, resembling the effect produced by marking the skin with a red crayon Erythema nodosum, and purpura, and increased capillary fragility may also be present, but all these skin manifestations may occur in the absence of rheumatic fever.

Non-traumatic epistaxis is common and may result in perforation of the nasal septum (page 147). Vague abdominal and precordial pain may also occur The abdominal pain may be localized to the right lower quadrant and when it is associated with vomiting and leucocytosis can simulate appendicitis. The pain may be due to inflammatory changes in the right rectus abdominalis muscle, or to inflammatory changes in the mesentery or to enlargement of the abdominal lymph glands.

ELECTROCARDIOGRAM

Prolongation of the *P–R* interval and prolongation of the *Q–T* interval often occur during the course of acute rheumatic fever, but even when present, are not specific for rheumatic fever. *T* wave changes are also not specific, but *RS–T* deviations characteristic of myocardial injury indicate the presence of a complicating pericarditis An irregular rhythm due to incomplete or complete *a–v* block, or *a–v* dissociation with interference, or auricular fibrillation or premature beats may also occur.

LABORATORY TESTS

There are no specific laboratory tests for rheumatic fever, although many abnormal findings may be present.

Erythrocyte Sedimentation Rate.—A rapid sedimentation rate usually occurs with rheumatic activity, and some investigators have used the sedimentation rate as a guide not only to diagnosis, but to therapy, accepting a rapid rate as proof of activity. However, I have seen cases of acute rheumatic fever where the sedimentation rate was normal. This is particularly so if cardiac decompensation is present. On the other hand, a rapid

sedimentation rate occurs in many toxic and infectious conditions in addition to rheumatic fever and rheumatoid arthritis

White Blood Count.—There is usually elevation of the white blood count with an increase in polymorphonuclear cells and a shift to the left The white blood count may reach 25,000, but in other cases, may remain below 10,000. When elevated, the count slowly returns to normal over a period of weeks or longer.

Red Blood Count.—A moderate and often persistent microcytic anemia with the hemoglobin falling even to 8 grams, often occurs during rheumatic activity, but this is not specific for rheumatic fever.

Antistreptolysin and Antifibrinolysin Titers.—These titers are often elevated but this merely indicates the presence of a streptococcal infection and is not specific for rheumatic fever In addition, the titers may remain normal even during an attack of rheumatic fever When elevated, they may remain high for many months. The chief value of the antistreptolysin titer test is that it is not elevated in acute rheumatoid arthritis but it usually is elevated in rheumatic fever

C-reactive Protein.—An abnormal protein may appear in the blood in response to many acute inflammations and acute infections. Since this protein is able to form a precipitate with the C-polysaccharide obtained from the pneumococcus, it has been called a C-reactive protein (CRP) Minute amounts of this protein may be demonstrated in human serum by a precipitin test using a specific antiserum obtained from rabbits which have been hyperimmunized by repeated injections of purified C-reactive protein.

Acute rheumatic fever is one of the conditions which causes the appearance of the C-reactive protein C-reactive protein is usually present during the acute phases of rheumatic fever It is also usually present during the stage of low-grade rheumatic activity It disappears during the course of treatment For example, it may disappear within one week after ACTH is started. However, a negative test for C-reactive protein is not necessarily an indication that rheumatic activity has ceased, but merely means that the body is responding to the drug therapy (ACTH, cortisone, salicylates). (A similar situation holds for the decrease in the sedimentation rate which occurs with steroid and salicylate therapy)

Although an elevation of the sedimentation rate and the presence of C-reactive protein occur together in many cases, they do not vary in identical ways and the C-reactive protein seems to be a more sensitive indicator of rheumatic activity than the sedimentation rate

In addition to being present in rheumatic fever, the C-reactive protein appears in subacute bacterial endocarditis and in some cases of acute myocardial infarction It also appears in many other conditions, such as pneumococcal pneumonia, staphylococcal infections, infections of the colon-typhoid group and in many other conditions which are characterized by an inflammatory reaction

Vital Capacity.—Even though clinical signs of left-sided heart failure may not be present, there is usually diminution of the vital capacity, even to 40 per cent or less of normal during an attack of rheumatic fever (see page 93 for normal values) However, measurement of the vital capacity in children below eight years is generally unsatisfactory.

DIAGNOSIS

From what has been said, it is obvious that the diagnosis of a mild case of rheumatic fever, or the determination of the persistence of rheumatic activity in a patient with rheumatic fever may be extremely difficult and may tax the diagnostic acumen of the physician. Before a diagnosis of rheumatic fever is made, at least one of the following major manifestations of rheumatic fever should be present:

1 Carditis, including cardiac enlargement, significant murmurs, pericarditis or congestive failure.
2 Polyarthritis or arthralgia, and fever.
3 Chorea
4 Subcutaneous nodules.

Signs of continued rheumatic activity may include: persistent elevation of the sedimentation rate or persistent leucocytosis; continued low-grade fever, progressive microcytic anemia, failure to gain weight or progressive loss of weight, easy fatigability; pallor out of proportion to the level of hemoglobin, persistent tachycardia, especially during sleep, *etc* However, it should be stressed again that no one of these criteria is specific in indicating the presence or absence of rheumatic activity, and in the final analysis, each patient must be judged as an individual problem

The clinical picture of rheumatic fever can be simulated by the following conditions:

1 **Subacute Bacterial Endocarditis.**—Here, the temperature range is usually wider than in rheumatic fever, the joint manifestations less marked, a "café-au-lait" complexion may be present (page 508), as well as severe anemia. Clubbing of the fingers occurs early, and splenomegaly, petechiæ and other embolic phenomena, and a positive blood culture are found. Subacute bacterial endocarditis is rare in patients with long-standing rheumatic heart disease and auricular fibrillation However, both subacute bacterial endocarditis and rheumatic activity may occur simultaneously.

2 **Acute Rheumatoid Arthritis.**—Acute rheumatoid arthritis may simulate rheumatic fever, especially in adults. Subcutaneous nodules, an elevated sedimentation rate and a leucocytosis also occur in both conditions Laboratory tests may be valuable in differentiation, because agglutination tests for hemolytic streptococci are positive in rheumatoid arthritis, and negative in rheumatic fever, whereas the antistreptolysin titer usually rises in rheumatic fever, but remains low in rheumatoid arthritis There is no relation between the onset of acute rheumatoid arthritis and a preceding upper respiratory infection, unlike in acute rheumatic fever, and the pain and local inflammation of the joints in rheumatoid arthritis either does not respond or responds poorly to the antirheumatic drugs, whereas the response in rheumatic fever is excellent.

In the early stages, roentgenological signs of rheumatoid arthritis are absent, but in the subacute stages, generalized decalcification, narrowing of the joint spaces, and even beginning marginal reabsorption of bone may already be evident. In the later stages, ankylosis occurs, which is absent in rheumatic fever.

In rheumatoid arthritis, cardiovascular signs are usually absent, except for tachycardia. However, several studies have indicated that a high percentage of patients with rheumatoid arthritis at autopsy show cardiac lesions, including valvular deformities, typical of rheumatic fever As a matter of fact, many investigators believe that rheumatic fever and rheumatoid arthritis are merely different aspects of the same disease process

3 **Still's Disease.**—This is a term applied to what probably is a juvenile form of rheumatoid arthritis. The joints have the same appearance as in rheumatoid arthritis

4 **Lupus Erythematosus.**—This occurs particularly in young women, during the period of puberty to the menopause Long-continued, low-grade fever, leucopenia, involvement of the heart with an atypical verrucous endocarditis, inflammation of the serous cavities (pericardium, pleura, peritoneum) involvement of the kidney, including microscopic albuminuria and hematuria, with or without casts, arthralgia or even a polyarthritis, skin manifestations, including a butterfly rash over the bridge of the nose and face, and eventually death, are characteristic of lupus erythematosus (page 517)

COURSE AND PROGNOSIS

Death during an attack of acute rheumatic fever only occurs in about 10 per cent of cases. However, in the majority of patients, recurrent attacks of activity, scarring of the valves and the resultant cardiac hypertrophy and dilatation result in death due to congestive heart failure at an early age. Swift stated some years ago that the mean life of a patient with rheumatic fever was fifteen years after the first attack, and five years after the first bout of cardiac decompensation With the earlier recognition of rheumatic fever and better controlled therapy to-day, the outlook is not quite so gloomy, and a good percentage of patients may live beyond forty-five years Even if cardiac decompensation does not occur, there is the ever present danger of subacute bacterial endocarditis, which in the past was responsible for many deaths. Modern antibiotic therapy, however, has helped save most of the patients so afflicted

Recurrences are most common the year after the first attack. Thereafter, the chances for recurrence become markedly lessened Similarly, the danger of recurrence is greatest in children under thirteen, where the recurrence rate is 1 in 4, whereas, after the age of sixteen, the danger of recurrence decreases to 1 in 20

PROPHYLAXIS

There are now two effective methods of preventing rheumatic fever or its recurrences:

A Prompt treatment of a streptococcal infection in a patient with rheumatic heart disease with one of the antibiotic drugs

In any patient who has had rheumatic fever in the past, prompt antibiotic therapy should be begun when the following symptoms or signs appear:

Symptoms·

a Sore throat—onset sudden—in the tonsillar area, not in the trachea

b. Headache is common

c. Fever is variable; generally it is from 101° to 104° F.

d. Abdominal pain is common, especially in children.

e. Nausea and vomiting are common in children.

f. The following symptoms are usually *not* present: simple coryza cough, or hoarseness.

Signs.

a. The throat is red, frequently beefy red, but if seen early the redness may be mild.

b. A tonsillar exudate is usually present.

c. The tonsillar glands at the angle of the jaw are swollen and tender.

d. A scarlatinal rash may or may not be present. It usually is absent.

Laboratory Tests.

a. The white blood count is generally over 12,000, and in children often over 20,000.

b. Throat culture is positive for hemolytic streptococci.

Penicillin should be started as soon as possible. Children can be given 300,000 units of procaine aqueous penicillin intramuscularly in one dose daily for ten days. Adults should be given one dose of 600,000 units daily for ten to fourteen days.

If oral penicillin is used, children should be given 200,000 to 300,000 units one-half to one hour before each meal and at bedtime, for a daily total of 800,000 to 1.2 million units in four divided doses. Adults should be given 500,000 units four times a day. This dose schedule should be continued for ten days.

Aureomycin, terramycin or tetracycline, in a dose of 0.5 gram daily for children, and 1 gram daily for adults, in divided doses, every six hours can be used instead of penicillin, for ten days.

It is important to continue antibiotic therapy for the entire ten days even though the temperature may return to normal and the patient may feel better within one or two days. In this way, all the streptococci are killed.

Penicillin troches or lozenges, or sulfonamides should not be used in the treatment of the streptococcal infection.

Benzathine penicillin G in one intramuscular dose of 600,000 units for children, or 900,000 units for adults, or an intramuscular injection of procaine penicillin with aluminum monostearate in oil, in a dose of 300,000 units for children (600,000 units for adults), every third day for three doses can also be used.

B. Maintenance of continuous antibiotic therapy in a patient with rheumatic heart disease may prevent an initial infection by the group A streptococci.

Who should be treated? All patients under the age of eighteen who have had rheumatic fever or chorea at any time, and all those over eighteen who have had an attack within five years.

When should prophylactic treatment be started? At the end of the second week of the attack of rheumatic fever, or at any time thereafter, when the patient is first seen. If the patient is receiving cortisone or ACTH, be cautious that other infections are not masked, since the prophylactic dose is not adequate to treat a concurrent illness such as pneu-

Before the start of prophylaxis, the group A hemolytic streptococci should be eliminated by large doses of antibiotic therapy (see above)

How long should prophylaxis be continued? In children, up to the age of eighteen at least, and possibly for life In all those above this age, for at least five years from their last attack

Should prophylaxis be continued during the summer? Yes.

Prophylactic Methods.—Oral penicillin can be given in a dose of 250,000 units one-half an hour to one hour before breakfast, and at bedtime.

Toxic reactions to penicillin may occur These may include urticaria, reactions similar to serum sickness, including fever, and joint pains which may simulate rheumatic fever, or angioneurotic edema If any of these occurs, the penicillin should be stopped

Recent studies indicate that one intramuscular injection monthly of 1,200,000 units of Bicillin (Benzathine Penicillin G), a new repository penicillin preparation, may also be effective for rheumatic fever prophylaxis

The broad spectrum antibiotics should *not* be used for long-term prophylaxis of rheumatic fever.

TREATMENT

The treatment of rheumatic fever is still largely empirical and symptomatic in spite of the use of the steroids such as cortisone or hydrocortisone, or corticotropin (ACTH) As a matter of fact, there is much evidence that the pharmacological action of the steroid hormones and the salicylates is similar in many respects For example, the steroids and the salicylates both cause a fall in circulating eosinophiles, both cause an increase in urinary 17-ketosteroids, both have an anti-inflammatory effect on experimental arthritis, both have an antipyretic and analgesic effect, both cause a significant decrease in the sedimentation rate, both cause an increased urinary excretion of uric acid, both have a catabolic effect, both inhibit the spreading phenomenon produced by hyaluronidase, both can decrease the skin reaction of experimentally induced Arthus' phenomena, both can modify anaphylactic shock, and it has been reported that salicylates can produce the signs of a mild Cushing's syndrome

There are, of course, marked differences between the steroids and the salicylates, but in the average case of acute rheumatic fever it is questionable whether steroid therapy has any advantage over salicylate therapy I have seen an occasional case of acute rheumatic fever which did not respond to cortisone or ACTH, but which did respond to salicylates However, in some cases of chronic, active rheumatic fever, the steroids may be life-saving

Salicylates.—The salicylates are extremely important in the treatment of acute rheumatic fever because they alleviate pain, hasten the absorption of joint and other transudates and exudates, and have an antipyretic action. There is also some evidence that the salicylates may have a specific antirheumatic effect. To obtain a therapeutic effect in rheumatic fever, plasma salicylate levels up to 35 mg per cent or more may be needed. Good plasma salicylate levels can be obtained with the oral administration of aspirin (acetylsalicylic acid), or sodium salicylate

The average daily dose of aspirin or sodium salicylate for a child is 3 to 6 grams (45 to 90 grains), for an adult, 4 to 10 grams (60 to 150 grains), given in divided doses, every four hours, day and night

When sodium salicylate is prescribed, an equal amount of sodium bicarbonate (or a mixture of sodium and potassium bicarbonate) should be given to prevent gastric irritation However, the bicarbonate tends to decrease the plasma salicylate level by decreasing absorption of the salicylate from the stomach and by increasing renal excretion of the salicylate. When aspirin, which I prefer, is used, bicarbonate is unnecessary.

Aspirin can be prescribed in the form of ordinary 0.33 gram (5 grain) tablets, or in powder form. Sodium salicylate can be prescribed in powder form, using the following prescription, which provides 1 gram with each dose

℞

Sodium Salicylate	30
Sodium Bicarbonate	
Potassium bicarbonate aa	15

Div in Cht ad no 30.
S Dissolve one powder in a glass of carbonated water every four hours

For those who cannot tolerate salicylates orally, the drug can be given rectally in similar doses. The patient should receive a preliminary enema of sodium bicarbonate (1 teaspoon to 1 pint of water). Then 3 grams of *sodium salicylate is dissolved in 120 cc (4 ounces) of a weak starch solution,* and given rectally twice daily

If in spite of large doses of salicylates, symptoms do not abate, and the plasma salicylate level remains low, para-aminobenzoic acid can be prescribed in conjunction with the salicylates to raise the plasma salicylate level A daily dose of 24 grams of para-aminobenzoic acid in an adult will double the plasma salicylate level. Children require proportionately smaller doses

Sodium salicylate has also been given intravenously, 10 grams dissolved in 1000 cc. of physiological saline (a 1 per cent solution), allowed to run in slowly over a period of four to six hours However, the danger of salicylism developing with such large doses is very great

Salicylism, or salicylate toxicity, is manifested in the following ways early toxic symptoms include fullness in the head or headache and dizziness, or tinnitus Nausea and vomiting and even diarrhea may occur. The drug need not be discontinued because of these symptoms, but the dose should be reduced

The most serious sign of salicylate intoxication is *hyperventilation* This is accompanied by acidosis with a decreased carbon dioxide and bicarbonate level in the blood and a plasma salicylate level of about 50 mg. per cent. Salicylate hyperventilation should not be confused with the dyspnea of heart failure. In hyperventilation, the patient takes deep and rapid breaths and yet does not have any subjective symptoms of difficulty of breathing Usually he can lie flat in bed. The urine may or may not contain acetone

Salicylate therapy should be stopped immediately if hyperventilation develops. If the drug is continued, apathy, drowsiness, dimness of vision, mental confusion, stupor, coma, even respiratory failure and death may occur.

Other toxic signs include a drug fever, especially in children, and blotchy, erythematous or eczematous skin eruptions

Another complication that may result from salicylate therapy is a prolongation of the prothrombin time. This may cause hemorrhagic phenomena. However, this can be prevented by giving synthetic vitamin K. One milligram will counteract the prothrombin-reducing action of 1 gram of aspirin.

Because the salicylates may have a specific anti-rheumatic effect, they should be continued for six or more weeks

Cortisone and ACTH.—The theoretical use of the adrenal cortical hormone, cortisone (17-hydroxy-11-dehydroxycorticosterone, compound E, cortone), and the pituitary adrenocorticotrophic hormone, ACTH, in the treatment of rheumatic fever and other collagen diseases, rests on the observations that these substances are able to depress the activity of the mesenchymal tissues, which are principally involved in the collagen diseases For example, when used in cases of rheumatic fever, a marked reduction inthe serum concentration of gamma globulin and in antistreptolysin-O titer occur, and a similar reduction in gamma globulin occurs in treated cases of lupus erythematosus In addition, as I mentioned above, ACTH and cortisone can prevent or modify experimental anaphylactic and histamine reactions, which is significant if one accepts the theory that rheumatic fever and allied diseases are allergic in nature (see page 483)

ACTH (Corticotropin) —Since the effect of ACTH varies greatly in different persons, no fixed dose schedule can be described (The pharmacological effect of ACTH can be determined by its ability to lower the blood eosinophile level, just like cortisone) In general, an effective therapeutic response can ordinarily be produced by a total daily dose of 40 to 80 units of the original short-acting ACTH preparations, administered in divided doses at intervals of six to eight hours In some cases, as much as 200 units daily may be needed. If more than 100 mg daily is used for long periods, cumulation and undesirable physiological or metabolic effects frequently appear. Therefore, once a satisfactory clinical remission has been obtained, the total daily dosage of ACTH should be reduced to the minimal level capable of maintaining the patient's improvement For example, individual doses may be reduced by 5 units daily at intervals of three to five days, until a satisfactory maintenance schedule is established (In some cases, the patient may become refractory to intramuscular ACTH This phenomenon has been called *ACTH resistance*)

ACTH gel, which is a long-acting preparation of ACTH in a gelatin menstruum, is now available and preferable to the short-acting ACTH in the treatment of rheumatic fever The maximal effect of ACTH gel occurs from fifteen to eighteen hours after injection and the total duration of its effect lasts more than twenty-four hours Therefore, one intramuscular or subcutaneous injection daily may be sufficient

A simple way to use ACTH gel is as follows: for young children (weighing forty pounds or less), 40 clinical units daily can be given in one injection For older and heavier children, 60 units are given once daily.

This dose should be continued for the first three to four weeks. (Cumulation occurs and the dose may have to be decreased sooner.) After this,

Bed Rest.—Absolute bed rest is extremely important during the acute phase of the disease, especially if overt signs of acute carditis are present. Rest in bed should be continued until the signs of rheumatic activity disappear. This usually takes five or six weeks but may be longer. However, the problem of deciding when rheumatic activity has subsided is sometimes very difficult, and it may be necessary to allow the child up even if the sedimentation rate is slightly elevated or if there is a persistent leucocytosis, or even if a low-grade fever is present, if the clinical impression is favorable. One should not forget that the persistence of a low-grade fever, and an elevated sedimentation rate may not be due to rheumatic activity but to a chronic sinusitis or tonsillitis as Jackson and others have pointed out

The Treatment of Acute Carditis.—In addition to bed rest, acute carditis should be treated with oxygen which may be helpful in relieving restlessness, cyanosis, dyspnea and even the tachycardia. Digitalis is of little value, possibly because the heart failure is due to toxic rather than mechanical factors. In addition, even small doses of digitalis may precipitate signs of severe digitalis toxicity in children (coupled premature contractions, auricular fibrillation or flutter, *a-v* block, ventricular tachycardia) and may cause death, so that if used, only small doses of the digitalis preparations should be prescribed (see page 263). A low-sodium diet (page 248), and the mercurial and xanthine diuretics (pages 250 and 254) are much more valuable In this connection, aspirin is preferable to the use of sodium salicylate and sodium bicarbonate especially when heart failure is present, because the sodium ion can aggravate the heart failure (see page 129).

The treatment of pericarditis is the same as that for uncomplicated carditis. Large doses of the salicylates may be very helpful in causing pericardial effusion to subside It is very rarely necessary to tap the pericardium.

Other Therapy.—During the acute phase of the polyarthritis, swathing the joints with cotton pads, support of the limbs in slight flexion, and even the use of a cradle to keep the weight of blankets off painful limbs may be necessary. Local use of oil of wintergreen (methyl salicylate) may also be of some help.

Sulfa drugs and penicillin are not only valueless once the active stage of rheumatic fever appears, but may aggravate the rheumatic fever and are contraindicated.

A diet high in calories should be given, supplemented with vitamins A, C and D, if the child is undernourished (5000 units vitamin A, 400 units vitamin D, and 100 mg. ascorbic acid [vitamin C] daily). Massive doses of ascorbic acid or of vitamin P have not proved helpful in preventing purpuric manifestations or in correcting the increased capillary fragility which is commonly present

One to two eggs a day may also be helpful (see page 483).

Serums, vaccines, and the removal of foci of infection are worthless

If anemia is present, 0.6 to 1 gram (10 to 15 grains) of ferrous sulfate daily is usually helpful. In rare cases, small repeated transfusions may be necessary, but in the presence of acute carditis not more than 100 cc. of blood should be transfused at one time in a child, and not more than 250 cc in an adult.

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A simple way to use ACTH gel is as follows: for young children (weighing forty pounds or less), 40 clinical units daily can be given in one injection For older and heavier children, 60 units are given once daily

This dose should be continued for the first three to four weeks (Cumulation occurs and the dose may have to be decreased sooner.) After this,

the dose can gradually be decreased and then stopped after six to eight or more weeks of therapy

ACTH gel is supplied in multiple dose vials, in concentrations of 20, 40 and 80 units per cc. (An insulin syringe can be used to measure the dose for injection)

ACTH and cortisone are equally effective in the treatment of rheumatic fever

Cortisone is supplied as the acetate salt in 5 and 25 mg. tablets, for oral use and as a microcrystalline suspension in saline for intramuscular injection, each cc. containing 25 or 50 mg. Oral therapy is as effective as intramuscular therapy.

The maximal effect of cortisone by mouth is obtained within four to eight hours and rapidly declines (This can be measured by studying the decrease in blood eosinophiles, using a special diluent and counting chamber.) However, when cortisone is given intramuscularly, it is slowly absorbed, its action lasts twenty-four hours and after prolonged therapy, cumulation occurs, so that an effect continues for at least three days after the drug is discontinued. Part is excreted unchanged in the urine; part is converted to 17-ketosteroids and then excreted. Cortisone does not stimulate the adrenals and may actually suppress the secretion of adrenal steroids because it inhibits pituitary ACTH production

The optimum dose of cortisone in the treatment of rheumatic fever has not yet been completely established and appears to be related to the severity of the illness rather than to age. The following dose schedule is usually effective: Up to 400 mg. of cortisone can be given orally (100 mg every six hours) the first day. From the second day on, a daily dose of 200 mg is given until a satisfactory response is obtained. Then, the dose is reduced step-wise by 25 mg. every day or two, to a daily dose of 100 mg or less, which is continued for six to eight weeks or longer.

Hydrocortisone (hydrocortone, compound F, cortef) can be used in place of cortisone Since it is approximately one and a half times more potent than cortisone, the first daily dose should be approximately 260 mg. (eight 20 mg tablets), given in divided doses, every six hours. From the second day on, a daily dose of 130 mg. can be used, until a satisfactory response is obtained Then, the dosage is gradually reduced in steps of 5 to 10 mg. daily, to a daily dose of 60 mg or less, for six to eight weeks or longer. Finally, the dose is still further decreased and stopped in a period of three days

Hydrocortisone acetate is supplied in tablets of 5, 10, and 20 mg. strength.

If a patient who is receiving cortisone or hydrocortisone requires emergency surgery, additional quantities are needed. For immediate adrenal cortical support, 30 to 50 cc of aqueous adrenal cortical extract can be given intravenously. In addition, hydrocortisone in a daily dose of 70 to 140 mg (or 100 to 200 mg. of cortisone) should be given, depending on the dosage prior to surgery, and the nature of the surgical procedure to be performed The dosage should be gradually reduced in four or five days after the operation.

A slight exacerbation of the disease process may appear for a period of a week or more after either drug is stopped. This does not mean that therapy

should be resumed, but if the child develops frank signs of rheumatic activity, either cortisone or ACTH therapy should be resumed

It should be emphasized that neither cortisone nor ACTH cures rheumatic fever, not do the drugs shorten the duration of the state of rheumatic activity. They merely prevent intense exudative and inflammatory reactions in the body and therefore prevent the fibroblast proliferation and subsequent scarring of such vulnerable tissues as the cardiac valves, which ordinarily follows For this reason, the drugs must be continued until the rheumatic process runs its natural course and subsides For a similar reason, the drugs have been most successful in the first or second attack of rheumatic fever, and the results, for the most part, have been disappointing in cases of chronically active rheumatic fever with severe valve damage and heart failure.

Side Effects—Most of the untoward effects of ACTH and cortisone are extensions of their physiological actions, and may result in the characteristic Cushing syndrome (see page 694), or in isolated abnormalities For example, the drugs induce a reduction in the utilization of carbohydrate and interfere with the action of insulin which may actually result in frank diabetes mellitus, and may require the use of insulin The high level of circulating adrenal cortical steroids which occurs may depress gonadal function, and menstruation may be delayed or inhibited Hirsutism of the body, acne of the face and neck, and loss of scalp hair may occasionally occur

Retention of sodium, chloride and water are common with ACTH, rarer with cortisone. This may be manifested by a progressive gain in weight, which may result in edema and other signs of congestive heart failure or pulmonary edema This usually appears during the first week of therapy and can be alleviated or prevented by a low-sodium diet (page 248) or by the use of cortisone instead of ACTH, especially in patients who already have heart failure Mercurials can also be used with precautions (see below)

ACTH can also cause an abnormal elevation of blood pressure, cortisone practically never raises the blood pressure abnormally Both drugs cause a lowering of blood potassium and chloride and alkalosis In addition, marked muscular weakness or paralysis may occur because of the loss of potassium. These symptoms can be prevented or ameliorated by the oral administration of potassium chloride, 1 to 3 grams (in enteric coated tablets) 3 times a day, especially if mercurial diuretics are used because the mercurials cause a marked excretion of potassium in the urine Both drugs increase urinary nitrogen excretion, thereby producing a negative nitrogen balance Mental changes are common, especially euphoria However, excitement, mania, and occasionally severe mental depression or convulsions may occur.

ACTH is contraindicated in diabetes mellitus, congestive heart failure, hypertensive heart disease, Cushing's syndrome, acne, hirsutism, osteoporosis and osteomalacia The use of cortisone is similarly limited with the exception of hypertensive heart disease. However, in a disease such as lupus erythematosus, or periarteritis nodosa, which would be otherwise fatal, use of the drugs would be advisable even though one of the above contraindications were present

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The Treatment of Chorea.—Fever therapy has proven helpful in chorea The daily injection of typhoid-paratyphoid vaccine has been used for one week, beginning with 0 1 cc intravenously, to raise the temperature to 105° or 106°. The child should be well wrapped in blankets Within twenty minutes a chill usually occurs, and the temperature begins to rise It continues to rise for two to four hours, remains at a peak for one hour and then falls If the temperature rises to 106°, 5 grains of aspirin should be given and an ice bag applied to the head Codeine can be given if headache develops. The only danger of fever therapy is that it may precipitate a recurrence of polyarthritis or carditis For this reason, cortisone or ACTH may be preferable

Nonspecific therapy for chorea, consisting of rest in bed and sedatives is also helpful

The Treatment of Convalescence.—When signs of rheumatic activity disappear, in other words, when the temperature remains normal without medication, and when the symptoms and signs of infection have disappeared, the inactive stage, and convalescence can be said to have begun However, during the period of convalescence, the patient may actually be in a prolonged phase of quiescent or subclinical activity.

Convalescence should be continued for several months before the patient is permitted to go back to work or to school During this period, removal of the patient to a warm climate is beneficial Convalescent care is sometimes difficult to obtain at home, and it may be advisable to send the child to a reputable convalescent home for rheumatic children However, at such homes, there is always the danger that an epidemic of streptococcic etiology will develop, causing a recurrence of rheumatic fever

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Chapter 32

BACTERIAL ENDOCARDITIS

In bacterial endocarditis, the endocardium of the heart, including the valves are invaded by virulent organisms. In the past it has been customary to divide bacterial endocarditis into two groups, acute bacterial endocarditis, and subacute bacterial endocarditis, depending on whether the disease runs its course (with death or recovery) in six weeks This classification is not completely satisfactory, because the same organism, such as the hemophilus influenzæ may produce an acute bacterial endocarditis in one patient, and a subacute bacterial endocarditis in another However, there are sufficient differences between the two groups to warrant retention of the classification.

ACUTE BACTERIAL ENDOCARDITIS

Acute bacterial endocarditis may occur during the course of a systemic infection, such as pneumonia, meningitis, puerperal sepsis, *etc.*, but may also occur after a mild localized infection, such as a skin furuncle, or gonorrhea, *etc* Practically any virulent pyogenic organism can produce an acute bacterial endocarditis, the most common are. group A streptococci, staphylococcus aureus, escherichia coli, pneumococcus, meningococcus, gonococcus and hemophilus influenzæ

Pathology.—The pathological changes are similar to those which occur in subacute bacterial endocarditis (page 505) and consist of the development of infected verrucæ on the valves and adjacent structures of the heart. However, in acute bacterial endocarditis, normal valves are usually invaded, unlike in subacute bacterial endocarditis The mitral and aortic valves are most commonly affected, the tricuspid valve less frequently, and the pulmonary valve rarely The site of implantation of the bacteria is determined chiefly by mechanical factors, the bacteria settling on the valves that carry the greatest load.

Symptoms.—Since acute bacterial endocarditis is essentially a complication of septicemia, the symptoms are those of septicemia, namely: severe prostration with muscular and bone pains, chills, fever which may remain high, or may be remittent, spiking to 105° or higher in the evening and dropping almost to normal in the morning However, the fever may be intermittent, with periods of normal temperature alternating with the fever. Cerebral symptoms, such as headache, lethargy, even delirium or coma may occur. Abdominal symptoms such as nausea and vomiting, even diarrhea are common.

The onset of these symptoms may occur with violent abruptness, as for example in a case of staphylococcus endocarditis resulting from an insignifi-

cant cutaneous infection. In other cases, such as endocarditis complicating a severe pneumonia, it may be difficult to determine the onset of the septicemia and the endocarditis

Signs.—Signs of septicemia, such as marked leucocytosis, moderate secondary anemia, tachycardia, enlargement of the spleen, and embolic manifestations in the skin, and internal organs such as the brain, lungs, kidneys, spleen, *etc*, are common The source of these emboli may be fragments of the verrucæ, but emboli may occur from clumps of bacteria floating free in the blood stream even in the absence of an endocarditis. Febrile albuminuria is common, but signs of acute nephritis are rare except in subacute bacterial endocarditis However, infarction of the kidney may result in microscopic hematuria

The only sign pointing directly to the endocardium is the development of murmurs, either systolic or diastolic, in the mitral or aortic valve area. These murmurs vary in intensity from day to day.

Diagnosis.—Diagnosis is made from a positive blood culture (page 507) and the presence of cardiac murmurs A diagnosis of septicemia can be made from a positive blood culture, but a diagnosis of acute bacterial endocarditis is not justified unless a murmur is present. However, a soft apical systolic murmur may occur with the fever and tachycardia, even if endocarditis is not present

Course and Prognosis.—Death may occur rapidly in the course of a few days or within six weeks in most cases, unless specific antibiotic therapy is used Death may occur from toxemia, rarely from the development of an acute carditis, or as a result of emboli to the brain, lungs or other vital organs

Treatment.—Treatment is the same as for subacute bacterial endocarditis (page 508).

SUBACUTE BACTERIAL ENDOCARDITIS

Subacute bacterial endocarditis (endocarditis lenta, chronic ulcerative endocarditis), unlike acute bacterial endocarditis is usually superimposed on a valve scarred from rheumatic fever, rarely from syphilis, or the endocarditis is superimposed on a valve congenitally deformed (bicuspid aortic valve, pulmonary stenosis), or develops at the site of a congenital lesion, such as a patent ductus arteriosus, coarctation of the aorta, interventricular septal defects, *etc.* (Patients with interauricular septal defects rarely develop subacute bacterial endocarditis) In rare instances, subacute bacterial endocarditis occurs in a person with a previously normal heart, or becomes engrafted on an arteriovenous fistula.

Another difference between subacute and acute bacterial endocarditis is that subacute bacterial endocarditis is caused by organisms of low virulence Varieties of the streptococcus viridans (streptococcus salivarius, streptococcus mitis, streptococcus sanguis [s b e]) and gamma streptococci are the causative agents in 90 per cent of the cases. (The streptococci viridans organisms, unlike the group A beta hemolytic streptococci may not produce a group-specific carbohydrate—see page 483.) Other streptococci which may cause a subacute bacterial endocarditis are group D streptococci (the

enterococcus or streptococcus faecalis) which are usually very resistant to penicillin, and occasionally group B or G streptococci In addition, a subacute bacterial endocarditis can be caused by hemophilus influenzæ, gonococcus, members of the genus Neisseria, staphylococcus, meningococcus, pseudodiphtheroids, brucella melitensis, anaerobic organisms, and by yeasts and other higher forms. Occasionally two infecting organisms are present simultaneously

The incidence of endocarditis due to streptococcus fecalis (enterococcus) and staphylococcus aureus has been increasing steadily

Pathology.—In both acute and subacute bacterial endocarditis, the endothelium of the valve leaflet is damaged by the deposition of verrucæ (vegetations) which consist of irregular masses of red and white blood cells, platelets, fibrin, deeply imbedded in which are the infecting bacteria. The verrucæ are larger than those which occur in acute rheumatic fever, and they may spread to the chordæ tendineæ and to the auricular and ventricular endocardium, where the verrucæ touch the walls of the heart The verrucæ may also spread to the aortic wall, from the aortic valve

The resultant inflammation of the valve may cause perforation or aneurismal dilatation of the valve leaflets Ulceration and even a mycotic (infective) aneurism of the aorta may result The interventricular septum may also become involved, with aneurismal outpocketing or perforation, and the conduction system may be injured, with *a–v* block resulting The vegetations on the aortic valve may proliferate so much as to block the mouths of the coronary arteries

Pericardial involvement is very rare Myocarditis, however, is common, and a typical but not specific lesion, consisting of infiltration of the myocardium with mononuclear cells (Bracht-Wachter bodies) may occur Small myocardial abscesses, infarcts, and areas of diffuse inflammation in the heart may also occur.

Mycotic aneurisms of the arteries may develop They are usually small and are due to implantation of the organism on the intimal surface of the artery, especially at a point of bifurcation or branching. This results in arteritis, weakening of the arterial wall and an aneurism which may later rupture

In the kidney an embolic form of glomerulonephritis may develop Small bacterial emboli destroy one or more loops in some part of a glomerulus, resulting eventually in the formation of a characteristic fibrous plug in that part of the glomerulus In the early stages, the hemorrhages resulting from the multiple emboli give the surface of the kidney a "flea-bitten" appearance. The spleen shows a nonspecific reaction to the infection Splenic infarcts may also be present Elsewhere in the body and brain, the lesions are produced by multiple emboli

Etiology.—The bacteria may gain access to the valves by way of a transient bacteremia which may occur, for example, after tonsillectomy, extraction of teeth, childbirth, or surgical, especially genitourinary operations It is also possible that the bacteria are brought to the valve by way of the blood vessels and capillaries of the valves. This may be an important factor, because subacute bacterial endocarditis does not involve badly scarred and fibrosed valves, and is therefore not too common in patients

with chronic mitral stenosis and auricular fibrillation, or in patients who suffer from chronic congestive heart failure.

Subacute bacterial endocarditis may occur at any age group although it is rare in infancy. It is most common between the ages of fifteen and thirty years

Symptoms.—The symptoms of subacute bacterial endocarditis may be like those of acute bacterial endocarditis with chills, spiking fever, *etc.* More often the onset is insidious. The patient complains of anorexia, weakness, loss of weight and low-grade fever, which may not exceed 101° for weeks. Joint pains often are present, and the symptoms very closely resemble those of rheumatic fever. As a matter of fact, rheumatic fever and subacute bacterial endocarditis may be present simultaneously. In some cases, the first sign of illness is the development of embolic manifestations

Signs.—The signs of subacute bacterial endocarditis are: 1. The preexistence of an acquired valvular lesion or congenital heart disease. The murmurs, however, often change from day to day, or murmurs may develop while the patient is under observation. A soft apical systolic murmur is not significant, because it may occur in any febrile state. A rough systolic aortic or mitral murmur may appear as a result of the valvulitis, or from perforation of a valve leaflet, or from rupture of a chorda, *etc*

2 Fever, which may be low-grade, high, remittent, or intermittent.

3 Progressive, secondary hypochromic anemia. Marked pallor is usually present.

The presence of anemia, low-grade fever and a heart murmur should make one consider the diagnosis of subacute bacterial endocarditis. As a matter of fact, in the early stages of the endocarditis, the murmur may be absent, so that unexplained fever and anemia may be the earliest signs of the disease

4 Petechiæ may appear on the skin and mucous membranes (page 139)

5 Emboli to the skin may produce painful fingers and toes (page 139), Osler nodes (page 139), and Janeway lesions (page 139).

6 Moderate clubbing of the fingers (page 137) may appear even within a few weeks after the onset of the disease. The clubbing may disappear after therapy.

7. The spleen is enlarged but may or may not be palpable, especially in the early stages of the disease. In some cases, it may be tremendously enlarged

8. Tenderness of the lower sternum may occur when it is briskly tapped.

9. Signs and symptoms of emboli may be present. Infarction of the spleen is characterized by sudden left upper quadrant abdominal pain which may radiate to the left scapular region, and vomiting. A friction rub over the spleen may appear. Infarction of the kidney may produce gross hematuria—usually it is microscopic—and pain in the lumbar region, radiating to the inguinal region and the genitals. Infarction of the brain may produce hemiplegia, meningismus or even meningitis, signs suggestive of encephalitis, or abnormal psychotic behavior. Jaundice may appear after pulmonary infarction

10. Ophthalmoscopic examination may reveal hemorrhages, signs of retinitis, a choked disc, and round white spots (Roth's spots).

Electrocardiogram.—Nonspecific *T* wave changes and a prolonged *P–R* interval may appear. In rare cases, more advanced degrees of *a–v* block may develop. *RS–T* deviations typical of myocardial infarction may occur if an embolus occludes one of the major coronary arteries.

Laboratory Tests.—The most important laboratory test is the blood culture, because a positive culture can be obtained in from 85 to 95 per cent of the cases, if enough cultures are done At least 10 cc, even 20 cc of blood should be drawn, preferably during a period of high fever Multiple cultures should be made, certainly daily, and in problem cases, a positive culture is sometimes obtained by drawing blood every three hours for a period of twenty-four hours, in spite of the fact that previous single daily cultures had been negative. The reason for this is that the organisms enter the blood stream only intermittently Both aerobic and anaerobic cultures should be done and kept at least two weeks before being discarded as negative If penicillin is being used for therapy, its bacteriostatic effect must be inhibited by penicillinase, or a period of ninety-six hours allowed to elapse after the last dose of penicillin before blood is drawn for culture

In some cases, cultures of arterial blood or of sternal bone marrow may *be positive even when ordinary blood cultures are negative Another method that has been used to produce a positive culture is to inject 0.5 cc* of epinephrine (1–1000) subcutaneously about fifteen minutes before drawing blood The epinephrine causes contraction of the spleen and thus may produce the entrance of the bacteria into the blood stream

The blood may show a moderate leucocytosis of from 12,000 to 15,000, in addition to the anemia Differential white count may reveal a marked monocytosis, and in addition, large phagocytic cells, even 80 micra in diameter may be found (The average polymorphonuclear white cell has a diameter of 15 micra) Clumps of large endothelial cells may also appear in the peripheral blood The sedimentation rate is elevated The blood globulin level increases This may produce a false positive test for syphilis The urine may show microscopic hematuria and some albuminuria

Diagnosis.—Diagnosis is made from the signs of organic valvular or congenital heart disease, prolonged fever of varying degree, embolic phenomena and/or splenomegaly, and two successive positive blood cultures, because a transient bacteremia and a single positive blood culture may occur even in a normal person Such positive cultures are obtained from broth flasks, and not from blood agar plates, because the number of bacteria present is not sufficient to grow out on a plate Even if the blood culture is negative, treatment should be started after a week of observation if the other signs of endocarditis are present because if the endocarditis is confined to the right side of the heart positive cultures may never occur.

Rheumatic fever can simulate subacute bacterial endocarditis as was pointed out above, but in subacute bacterial endocarditis, the embolic phenomena, clubbed fingers, splenomegaly and positive blood culture allow differentiation to be made However, if rheumatic fever and subacute bacterial endocarditis are present simultaneously, the diagnosis of both the conditions may be difficult In such a case, temperature and joint manifestations may persist while the patient is on specific antibiotic therapy, and may respond to salicylates

Lupus erythematosus (page 516), blood dyscrasias, abdominal Hodgkin's disease, and obscure infections such as undulant fever, typhoid, malaria, tuberculosis, *etc*, can also simulate subacute bacterial endocarditis.

Course and Prognosis.—If untreated, less than 1 per cent of cases of subacute bacterial endocarditis recover. Death usually occurs in from six months to two years as a result of the bacterial infection, or from embolic complications, even myocardial infarction due to coronary artery embolization, or from active carditis or congestive heart failure, rarely from rupture of a mycotic aneurism.

Some patients who apparently recover may pass into what Libman has called the bacteria-free stage. This is characterized by progressive renal insufficiency, progressive anemia, marked splenomegaly, continued sterile embolization, and eventual death in about three and a half years. The patients are afebrile, but elevated temperatures may occur after infarction of the spleen, *etc* Such cases often show a characteristic brownish "café au lait" discoloration of the face and of the back of the hands.

With present-day antibiotic therapy, over 90 per cent of the patients can be cured Some patients die in spite of therapy because of embolic accidents Even in cases which have been cured by penicillin or other antibiotic therapy, sufficient scarring, deformity, perforation or mutilation of the valves or chordæ tendineæ may occur that death from congestive heart failure results in several months. The patient may also recover and become infected with another organism.

Prophylaxis.—In order to prevent a transient bacteremia in patients who are susceptible to subacute bacterial endocarditis (patients with rheumatic valvular disease or congenital heart disease), prophylactic therapy with penicillin should be given before minor or major surgical procedures and dental manipulations or extractions.

Recent experience indicates that massive doses of penicillin are necessary to prevent subacute bacterial endocarditis. For example, a daily injection of 600,000 units of a procaine-penicillin preparation for four to ten days prior to surgery, may be needed. In addition, the penicillin should be continued for five days after the surgical procedure.

Treatment.—Before treatment is started, the diagnosis should be established if possible by finding at least two positive blood cultures, as was pointed out above However, this may take a week or more. If the patient does not appear too ill, it is justifiable to wait a week for the results of blood cultures before starting antibiotic therapy. However, when the patient appears critically ill, it may be necessary to start therapy with penicillin at once, continuing, of course, to take multiple blood cultures to determine the responsible organism and its sensitivity to penicillin, streptomycin and other antibiotics.

The following is a list of the more commonly used antibiotics and the organisms against which they are effective:

Penicillin.
- Gram-positive microorganisms
- Gram-negative cocci

Streptomycin and Dihydrostreptomycin.
- Hemophilus parainfluenzæ

Klebsiella
Brucella (aureomycin should also be used)
Streptococcus fecalis (enterococcus) and other nonhemolytic streptococci (in combination with penicillin)

Aureomycin, Terramycin, Tetracycline
Penicillin-resistant staphylococci
Other penicillin-resistant bacteria
Streptobacillus moniliformis
Brucella (in combination with streptomycin)
Pasteurella
Other sensitive gram-negative organisms

Bacitracin (in combination with penicillin)
Staphylococci resistant to the above antibiotics
Streptococcus fecalis resistant to a combination of penicillin and streptomycin

Erythromycin or Magnamycin
Gram-positive organisms, especially staphylococci, which are resistant to all the above antibiotics

Neomycin
Proteus and other gram-negative organisms resistant to other antibiotics

Polymyxin B
Pseudomonas aeruginosa (pyocyaneus)

Sulfonamides (in combination with penicillin)
Meningococci

Penicillin Therapy.—Crystalline penicillin is the drug of choice in most cases of subacute bacterial endocarditis The amount of penicillin and the duration of therapy depend on the sensitivity of the organism to penicillin. The development of penicillin resistance is very rare

Penicillin sensitivity is expressed in terms of the smallest number of penicillin units per cc of the culture fluid required to inhibit the growth of the organism in vitro Sensitivity is determined by the serial dilution method of Fleming, or the Oxford cup method of Foster and Woodruff Organisms which can be inhibited with from 0 01 to 0 1 unit of penicillin/cc are considered sensitive Organisms which can be only inhibited with a penicillin concentration above 0 1 unit/cc are considered resistant In some resistant cases, it may require a penicillin concentration of 25 units/cc to inhibit growth in the in vitro tests

The in vitro sensitivity of the organism can be used to determine roughly the level to which the penicillin concentration in the blood should be elevated because, to effect a cure, it requires from 5 to 10 times the level needed for in vitro inhibition. In some cases even 200 times the in vitro inhibition level are needed to sterilize the blood. Penicillin blood levels are determined by the method of Rammelkamp. Thus, if the organism is inhibited in vitro by 0 1 unit of penicillin/cc, a blood level of 1 unit/cc should be obtained. This can be usually accomplished by a daily dose of penicillin of 1 million units given by constant intravenous drip, or 2 to 2.5 million units given in divided doses intramuscularly. An organism inhibited by 0 2 units/cc would therefore require approximately double this

dose However, regardless of the sensitivity of the organism, the daily dose of penicillin should not be less than 1 million units given intravenously, or 2 to 2.5 million units given intramuscularly in divided doses

When the sensitivity of the organism is from 0 5 to 10 units/cc., a daily dose of 5 to 10 million units of penicillin may be necessary, and for highly resistant strains which require from 10 to 25 units/cc. for in vitro inhibition, a daily dose of from 10 to 40 million units of penicillin may be needed, with or without benemid (see below). In such cases, combined penicillin and streptomycin therapy may be required

Penicillin can be given as follows:

For penicillin-sensitive organisms (0.1 unit/cc. or less), aqueous procaine penicillin is given intramuscularly in a daily dose of 2,400,000 units (1,200,000 units twice a day) for six weeks

If a satisfactory clinical improvement does not occur within a few days, the patient can be treated as if he had a penicillin-resistant organism (see below) Or, the dose of penicillin can be maintained, but 2 grams of benemid (see below) is given orally to increase the penicillin blood level

For endocarditis due to streptococcus fecalis (enterococcus), or other penicillin-resistant organisms, aqueous procaine penicillin is given intramuscularly, in a daily dose of 6 to 12 million units, in combination with 2 grams of streptomycin or dihydrostreptomycin daily (see below). The penicillin is given for six weeks, but the streptomycin or dihydrostreptomycin is stopped after four weeks to avoid toxicity. At this time, the dose of penicillin is increased to 12 million units (if less had been given) and 2 grams of benemid are given daily

If the patient is allergic to penicillin, serious allergic reactions can be avoided by giving an antihistaminic, such as 10 to 20 mg. of chlor-trimeton, intramuscularly, one-half an hour prior to each dose of penicillin.

The danger of procaine reactions is minimal. If collapse, due to circulatory depression occurs, epinephrine or other pressor drugs can be used If central nervous system irritability and convulsions occur, a 2½ per cent solution of pentothal sodium should be given intravenously.

When massive doses of penicillin are needed, the blood level can be raised by using benemid (probenecid), which interferes with the renal excretion of penicillin Most of the penicillin is excreted by way of the kidneys. Eighty per cent of this amount is excreted by the renal tubules and only 20 per cent by the glomeruli Both penicillin and benemid are excreted by the renal tubules by way of the same enzyme system Therefore, when benemid is being excreted, the penicillin is retained in the blood

Benemid is given orally in a daily dose of 2 to 4 grams (0.5 gram to 1 gram—1 to 2 tablets—four times a day). Such a dose can raise the blood penicillin level two- or threefold. Rarely, a drug rash or nausea may occur These reactions are not serious

Streptomycin and Dihydrostreptomycin.—Streptomycin, with or without dihydrostreptomycin, should not be used alone in the treatment of subacute bacterial endocarditis, but should be given in combination with penicillin

Streptomycin alone tends to damage the vestibular nerve Dihydrostreptomycin tends to damage the auditory nerve. However, toxicity can be avoided by using 2 grams of streptomycin daily for two weeks and then

continuing with 2 grams of dihydrostreptomycin daily for two weeks An alternative method is to give 1 gram of each daily for four weeks.

Aureomycin (Chlortetracycline), Terramycin (Oxytetracycline), Tetracycline (Tetracyn, Achromycin), and Chloramphenicol (Chloromycetin) — These broad spectrum antibiotics are bacteriostatic rather than bacteriocidal and should be used only when the organism does not respond to penicillin or streptomycin Even in such cases, the patient may show temporary improvement for a period of days or weeks, only to develop a fever again and other signs of the endocarditis This may occur even while the antibiotic is being given.

The broad spectrum antibiotics should not be given in combination with penicillin. However, they can be used in combination with streptomycin against brucella infections

An average effective daily dose is 1 to 2 grams orally, given in divided doses at six-hour intervals If necessary, they can be given parenterally Tetracycline, aureomycin and terramycin have practically identical chemical structures and can be used interchangeably Chloramphenicol (chloromycetin) should be used only in critically ill patients, because it may cause fatal hematological complications

Bacitracin.—Bacitracin can be used alone or in combination with penicillin against sensitive organisms. An average effective daily dose is 60,000 to 100,000 units, given intramuscularly in four divided doses It is more effective when given in combination with 6 to 12 million units of penicillin

Bacitracin is a potent antibiotic, but may cause kidney damage Before treatment is started, the urine should be examined for albumin, casts and cellular elements, and a blood urea nitrogen level determined The urine should be reexamined daily and the urea nitrogen test repeated twice a week The urine should be kept at a pH of 6 or higher by giving sodium bicarbonate or other alkalis

If the blood urea nitrogen is elevated to 25 mg per cent, bacitracin must be used very cautiously If during treatment the blood urea nitrogen rises to double its original level, the bacitracin should be stopped except under extraordinary conditions.

Bacitracin is supplied in rubber stoppered vials, each containing 60,000 units. It can be diluted in 1 or 2 per cent procaine to eliminate local pain at the site of injection

Bacitracin has been found particularly effective in cases of staphylococcal or enterococcus endocarditis which are resistant to penicillin and to the broad spectrum antibiotics

Erythromycin (Erythrocin, Ilotycin) is predominantly effective against the gram-positive organisms which are usually sensitive to penicillin Its major use is against penicillin-resistant staphylococci Side effects to erythromycin are rare In a few cases, depressed white blood counts have been noted

Erythromycin can be prescribed orally in the form of tablets containing 100 to 200 mg An effective daily dose for subacute bacterial endocarditis is from 1 2 to 1 6 grams, given in four doses, for four to six weeks Erythromycin should not be used alone in the treatment of subacute bacterial

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Chapter 33

DISSEMINATED LUPUS ERYTHEMATOSUS

DISSEMINATED lupus erythematosus is a generalized disease of the collagen tissue of the body. Its importance in cardiology is due to the fact that it can simulate both rheumatic fever and subacute bacterial endocarditis

Pathology.—The disturbances in collagen are noted most conspicuously in the smaller blood vessels of the viscera (heart, kidneys, lungs, liver, pancreas, skin, *etc.*) It causes proliferative lesions of the endothelium of the vessels, and degenerative and necrotic lesions of the vessel walls, associated with thrombi which often occlude the vessel lumen. In the kidneys, the changes may consist of proliferative, thrombotic or necrotic lesions of the glomerular loops In about half the cases, the glomeruli present a peculiar hyaline swelling of the collagen fibrils in the capillary walls. This may result in a characteristic thickening and stiffening of the capillary walls, so that the glomerular loops look rigid and thick, as if made of heavy bent wire, a picture which has been described as the "wire-loop lesion" Inflammatory pericardial, pleural and peritoneal exudation may also appear. In the skin, dilatation of the superficial vessels, edema of the cutis, atrophy of the epidermis, and liquefaction necrosis of the basal cell layer may occur The skin lesions attack particularly regions exposed to sunlight, such as the bridge of the nose, the malar eminences, and the extremities.

In about one-fourth of the cases, the heart shows a distinctive, nonbacterial type of valvulitis and endocarditis (the Libman-Sacks syndrome or atypical verrucous endocarditis) characterized by degeneration of the subendothelial collagenous tissue, which swells so as to form small sterile verrucæ These occur on both the auricular and ventricular surfaces of the valves, and may spread to the chordæ tendineæ and to the mural endocardium. All four valves may be involved The heart muscle remains uninvolved

Etiology.—The *cause of disseminated lupus erythematosus* is unknown. It is primarily a disease of women, in the premenopausal ages, and less than 5 per cent of the cases occur in males. Children, however, can be affected It is most commonly seen between the ages of twenty and forty years.

The disturbance of collagen which characterizes lupus erythematosus is similar in many respects to the pathological changes observed in allergic reactions, such as serum sickness, periarteritis nodosa, thrombo-angiitis obliterans, rheumatic fever, and diffuse scleroderma. All these conditions have been described by some investigators under the general term of diffuse vascular disease.

Symptoms.—The insidious onset with weakness, fever, and arthralgia resembles rheumatic fever or subacute bacterial endocarditis

Signs.—Some of the more common clinical signs are:

1. An erythematous, sometimes bluish, blotchy or confluent skin rash appears at one time or another in the course of the disease. Rarely, the rash may never appear. It is characteristically located on the bridge of the nose, extending in a butterfly pattern over the cheeks and the malar eminences. The shaded areas of the face and neck usually remain uninvolved. The rash is aggravated by sunlight. Small hemorrhages and telangiectasis may occur within the lesions, which are not limited to the face and may appear on the extremities. The mucous membranes of the mouth may also be involved with a macular eruption which may ulcerate. Purpuric lesions of the skin may also appear

2. A prolonged irregular fever is present, usually not septic in character. However, it may on occasion spike even to 105°, or there may be afebrile periods of months or longer.

3. Signs of serositis appear. The pericardium, pleura and even the peritoneum may be involved. There may be minimal effusion with pleural or pericardial friction rubs, or the effusion may be marked. Ascites, or abdominal pain, tenderness and rigidity may simulate an acute abdomen.

4. Cardiac involvement. Even in those cases with endocarditis, the cardiac signs may be minimal. Murmurs may or may not be present, and are usually nonspecific, due to the fever or anemia

Heart failure may also occur

5. Signs suggestive of emboli, such as white-centered petechiæ (page 139) and Osler nodes (page 139) may appear.

6. Arthralgia and even a polyarthritis, with redness and swelling of the joints may appear. Residual stiffness of the joints with limitation of motion, simulating even rheumatoid arthritis, may result.

7. Generalized lymphadenopathy may occur. The spleen is usually not palpable, but both liver and spleen may become enlarged

8. Ophthalmoscopic examination may show hemorrhages, exudates, even papilledema due to lesions of the retinal arteries

9. Pulmonary lesions. In addition to pleural effusions, a chronic interstitial pneumonitis is common. Clinically this may be observed as recurrent attacks of lobar or of patchy bronchopneumonia

10. Kidney involvement. Hematuria, proteinuria and a nephrotic or nephritic syndrome may occur.

11. Neurological and psychiatric disturbances are common. These may include hemiplegia, convulsions, or psychoses.

12. Occasionally a Raynaud syndrome occurs

Electrocardiogram.—Nonspecific *T* wave changes may occur. In addition, low voltage of the *QRS* complexes may develop as a result of pleural, pericardial or abdominal effusions

Laboratory Tests.—The blood shows a characteristic leukopenia, with the white blood count remaining 4000 or less even during a period of high fever. However, in the presence of secondary infections, a moderate leukocytosis may appear. A moderate or marked normocytic hypochromic anemia is present. The blood globulin level is elevated, especially the

euglobulin fraction, and a biologically false positive test for syphilis may result Thrombocytopenia is common, with or without purpura. The sedimentation rate is elevated. Blood culture is negative. The urine usually shows microscopic hematuria and albuminuria. Casts may or may not be present

The L.E. (Lupus Erythematosus) Cell and the L.E. Phenomenon—The L.E. phenomenon consists of rosettes of clumped white blood cells in association with a characteristic L.E cell. The L.E. cell is a mature polymorphonuclear leukocyte (rarely an eosinophile) which contains within it an inclusion body of homogeneous, nucleus-like material.

The L.E phenomenon and the L.E. cell can be demonstrated in both concentrated bone marrow and blood preparations. The following is a simple way in which the L.E. cell can be demonstrated from the clotted blood of patients with acute lupus erythematosus disseminatsous:

1. Draw 1 to 2 cc of venous blood. Let it coagulate in a clean, dry test tube and stand at body temperature for two hours

2 Centrifuge the tube for three minutes at 1500 r p.m., and remove the serum

3 Break up the clot by sticking a wooden applicator into it rapidly twenty to thirty times

4 Remove a drop of fluid from the broken clot. Smear it and stain with any standard hematologic stain, such as the Wright or Giemsa.

When the test is positive, at least one L.E. cell will be found in the first 300 cells counted

L.E cells are almost always observed during the acute stage of the disease, but may disappear during a remission or during steroid therapy. The finding of rosettes of clumped leucocytes is suggestive, but not pathognomonic of lupus erythematosus. The L.E. cell, however, is pathognomonic.

Diagnosis.—The appearance of prolonged fever, arthralgia, leucopenia, signs of inflammation of the serous membranes, a butterfly rash on the face, and a negative blood culture in a young woman are characteristic of disseminated lupus erythematosus. When the findings are not so obvious, the condition may simulate not only rheumatic fever and subacute bacterial endocarditis but periarteritis nodosa (see below), dermatomyositis, and diffuse scleroderma (page 520). It should be pointed out also that nonbacterial *thrombotic verrucæ can be found accidentally* post-mortem in patients with cachexia and otherwise normal hearts, the verrucæ having developed terminally

Diagnosis is confirmed by finding the L.E. cell in the blood or bone marrow However, a negative L.E test does not necessarily indicate that lupus erythematosus is not present. False positive tests have also been reported in cases of multiple myeloma, nephritis, *etc.* However, a false positive test is very rare

Occasionally, the first clue to lupus erythematosus is the development of a false positive serological test for syphilis.

A chronic form of lupus erythematosus, localized to the skin, and without systemic manifestations can also occur. There is no way of determining when the chronic discoid lupus erythematosus will develop systemic signs

Course and Prognosis.—Death usually occurs in about six months. However, spontaneous remissions even for years may occur, and rarely, spontaneous cures may occur Death usually occurs after a more or less protracted febrile course, often as the result of an intercurrent infection, such as pneumonia, and rarely from azotemia

Treatment.—Up to recently there has been no specific treatment for disseminated lupus erythematosus. However, remissions have been obtained with ACTH or cortisone (page 495), and it may be necessary to use one of these drugs indefinitely Spontaneous remissions also occur.

A general measure to be used is to protect the patient from sunlight as much as possible and to avoid exposure to ultraviolet light.

PERIARTERITIS NODOSA

Periarteritis nodosa (polyarteritis nodosa) is a disease of unknown etiology although there is evidence that it may be an anaphylactic type of hypersensitivity localized to the medium-sized arteries The media and adventitia show signs of marked inflammation and degeneration and the weakened arterial wall may give way, forming visible, nodular aneurisms. The inflammatory process may extend to the intima, causing thrombosis and occlusion of the vessel with resulting infarction of the area supplied by the vessel There is a predilection of the disease to affect the arteries of the heart, kidneys and gastrointestinal tract. The blood vessels of the lungs, brain, skin, muscles, *etc.*, may also be involved

The clinical picture depends on the organ system involved. Nonspecific manifestations include low-grade, irregular, remittent fever, marked prostration and weakness, weight loss, anemia, leucocytosis, occasionally eosinophilia, and a sterile blood culture

When the heart is involved, signs of cardiac enlargement and heart failure may appear, with edema and dyspnea; or pericarditis with or without effusion, or evidence of myocardial infarction due to occlusion of one of the coronary arteries. Rupture of a nodular coronary artery aneurism may result in hemopericardium

Hypertension is common This may be a point of differential diagnosis between periarteritis nodosa and lupus erythematosus, where hypotension rather than hypertension is common (unless the patient is receiving steroid therapy).

Involvement of the kidneys may cause edema, hematuria, albuminuria, casts, hypertension or uremia Involvement of the muscles and peripheral nerves may cause muscular pain, weakness and wasting, paresthesias, and paralysis of muscles Involvement of the gastrointestinal tract may cause anorexia, nausea, vomiting, diarrhea, or signs of intestinal obstruction due to occlusion of one of the mesenteric vessels Pulmonary involvement may cause asthma, cough, rales, and hemoptysis. Involvement of the retinal vessels may cause retinal hemorrhages and exudates Involvement of the joints may cause swelling, pain, and tenderness of the affected joint. Involvement of the liver can cause jaundice

A characteristic urinary sediment finding has been reported in cases of periarteritis nodosa This consists of red blood cells, red cell casts, oval

fat bodies, fatty and waxy casts, and frequently broad casts, all found in a single urine specimen.

The condition can be simulated by lupus erythematosus and other conditions with a chronic low-grade fever (see page 487). The course is usually slowly downhill with death occurring in a year or so. Occasionally, recovery occurs There has been no adequate specific treatment, but cortisone or ACTH should be used.

SCLERODERMA

Scleroderma is a collagen disease of unknown etiology It has sometimes been considered a vascular disorder because Raynaud's phenomenon usually precedes the scleroderma. Exacerbations of the disease are also related to periods of emotional conflict.

Etiology.—It has been suggested that the various collagen diseases, such as lupus erythematosus, periarteritis nodosa, scleroderma, dermatomyositis, platelet thrombosis are due to an antigen-antibody reaction occurring at different sites. Thus, if the antigen-antibody reaction occurs in a subintimal location in the blood vessels, platelet thrombosis occurs. Primary medial involvement results in periarteritis nodosa. If the antigen-antibody reaction occurs in the mesenchymal tissue, lupus erythematosus or scleroderma occurs.

Clinical Picture.—The earliest signs of scleroderma itself consists of stiffness and swelling of the skin. Vitiligo may occur, or hyperpigmentation Weakness, fever, a Raynaud's syndrome, and pain and stiffness of the joints of the extremities are common.

Scleroderma can also affect the heart. The collagen fibrils may compress the heart muscle cells which may become atrophic, and signs of progressive heart failure may appear. If the *a–v* node or the bundle of His is involved, *a–v* block may appear. The electrocardiogram may show nonspecific changes in the *RS–T* segment and *T* wave Involvement of the lungs may cause dyspnea and abnormal pulmonary findings. Involvement of the esophagus may cause dysphagia

Laboratory Tests.—There are no specific findings. An anemia may be present. The erythrocyte sedimentation rate may be elevated Hyperglobulinemia with a reversal of the a/g ratio may occur Serum calcium determinations are normal

X-Ray Examination.—Generalized enlargement of the heart may be present. The lung fields may show nodular abnormalities and linear streaking at the bases. Esophageal lesions, *ranging from* constriction to atony or dilatation may be present.

Bony changes may occur, consisting of demineralization of the terminal tufts with erosion of the finger tips Calcification of the soft tissues may also occur.

Treatment.—There is no effective treatment. Antibiotics, antihistaminics, testosterone, ACTH and cortisone and sympathectomy of the first to the twelfth thoracic segments have been used with some success Parathyroidectomy is no longer done.

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Chapter 34

RHEUMATIC HEART DISEASE

Introduction.—The absence of a history of rheumatic fever should not deter one from making a diagnosis of rheumatic heart disease if adequate physical and x-ray signs are present, because a definite history of rheumatic fever may be absent in as many as one-fourth the patients with chronic rheumatic heart disease. Then again, one should remember that rheumatic heart disease may occur as a sequel to scarlet fever.

After an attack of rheumatic carditis and valvulitis, the inflamed valves may heal without structural abnormalities and may completely return to normal However, valvular insufficiency or stenosis, or both, may occur.

Insufficiency (regurgitation, incompetency) of a valve occurs when the valve orifice is enlarged or complete closure of the valve is impossible. It can be produced by thickening and rigidity of the leaflets, which interfere with their closure, thus allowing blood to regurgitate when the valve should be closed Inflammatory changes and subsequent shortening of the chordæ tendineæ may also prevent the valve leaflets from closing completely

Stenosis of the valvular orifice occurs as a result of fusion of the valve leaflets at their commissures. This may also interfere with closure of the leaflets, so that insufficiency may occur along with the stenosis Although in most cases some degree of insufficiency and stenosis is present, "pure" stenosis and "pure" insufficiency may occur.

One valve or multiple valves may be involved. It is common to find an isolated mitral or aortic lesion, or combined mitral and aortic lesions. Isolated tricuspid or pulmonic lesions are very rare, and are usually found in conjunction with severe mitral and aortic lesions

In addition to the inflammatory lesions of the valve cusps, calcification of the valve cusps and of the annular ring (annulus fibrosus) of the valve may occur This is more common in the aortic valve than in the mitral valve. However, calcification of the annulus fibrosus alone may occur as a result of arteriosclerotic changes rather than as a result of rheumatic fever.

RHEUMATIC LESIONS OF THE MITRAL VALVE

Mitral Insufficiency.—Mitral insufficiency produces left auricular and left ventricular hypertrophy in the following way The blood regurgitating from the left ventricle to the left auricle during systole causes the left auricle to dilate, and eventually to hypertrophy because of the greater work required to propel the larger quantity of blood back to the ventricle. The work of the left ventricle is also increased because it must propel sufficient blood into the aorta for the needs of the body, in addition to using energy to propel the blood into the auricle through the insufficient mitral valve

Symptoms.—There are no symptoms produced by mitral insufficiency itself.

Signs.—*The presence of abnormal physical signs depends on the degree* of left ventricular hypertrophy. If it is minimal, physical signs may be normal with the exception of a soft or harsh, blowing apical systolic murmur. In such a case, the differentiation of this murmur from a normal apical systolic murmur is extremely difficult (page 166), and may be possible only by watching the patient over a period of years and noticing the progressive enlargement of the heart. In other cases, the apical impulse is forceful and displaced to the left and slightly downward, due to left ventricular hypertrophy.

Fluoroscopic and X-Ray Examination.—*The cardiac silhouette may appear* normal in the presence of minimal left ventricular hypertrophy. However, rounding of the left ventricle (page 181), and slight enlargement of the left auricle may be present.

A systolic expansion of the left auricle (page 190) may be present.

Catheterization Studies.—An early and high spiking systolic pulmonary capillary pressure curve *v* wave indicates mitral insufficiency. (The pulmonary capillary wedge pressure is a measure of the pressure in the left auricle—page 113).

Electrocardiogram.—*In the early stages of the disease, the tracing may* be normal. Later, the electrocardiogram may show signs of left ventricular hypertrophy or strain, or both (page 210). Auricular fibrillation is common.

Diagnosis.—*The difficulties in differentiating organic mitral insufficiency* from a normal apical systolic murmur have already been considered (page 166). Another source of difficulty lies in the differentiation of organic mitral insufficiency from apical systolic murmurs produced by relative insufficiency of the mitral valve, which may occur in hypertensive cardiovascular disease where the mitral ring is stretched by the enlarged left ventricle, or with the cardiac dilatation of congestive heart failure, or in febrile conditions, carditis or anemia. Arteriosclerotic calcification of the mitral annulus fibrosus may also produce mitral insufficiency. Mitral insufficiency *may also be due to uncommon conditions*. For example, acute or subacute bacterial endocarditis may heal, leaving a scarred and insufficient mitral valve, or one of the valve cusps or a chorda tendinea may rupture causing mitral insufficiency. Rarely syphilis or tuberculosis may involve the mitral valve. Myocardial infarction may cause rupture of one of the mitral papillary muscles.

The Diagnosis of Mitral Insufficiency in the Presence of Mitral Stenosis.—When mitral valve surgery is done for mitral stenosis, it is important to determine preoperatively if significant mitral insufficiency is present. This is often very difficult, because mitral insufficiency may be present with only a faint apical systolic murmur, and conversely, a tight mitral stenosis may be accompanied by a loud, apical systolic murmur.

The following criteria can be used to determine if mitral insufficiency is present in a patient who also has mitral stenosis:

1. *An apical systolic murmur of grade 3 or louder indicates a moderate* to marked mitral insufficiency.

2 Severe fatigability and weakness, rather than dyspnea are often associated with mitral insufficiency. However, these symptoms may be present in pure mitral stenosis, and absent in marked mitral insufficiency.

3. Definite left ventricular enlargement, demonstrated either by fluoroscopic or x-ray examination, or by electrocardiographic signs of left ventricular hypertrophy, are suggestive of predominant mitral insufficiency, if aortic valvular disease or hypertension is absent

4. An aneurismal dilatation of the left auricle also indicates mitral insufficiency.

5. Systolic expansion of the left auricle, especially in the P–A position, is a good sign of mitral insufficiency. In the R.A.O position, systolic expansion may occur in a patient with only mitral stenosis (page 190)

6 Auricular fibrillation is almost always present when mitral insufficiency complicates mitral stenosis. However, it may occur with pure mitral stenosis

7. Systemic embolization is very rare in mitral insufficiency Apparently, the regurgitant stream prevents stagnation of blood and thrombus formation in the left auricle.

8. Often the diagnosis of mitral insufficiency is made definitely by the surgeon when he feels the regurgitant systolic jet of blood hitting his finger in the left auricle Even this may be misleading. A weak or absent jet may occur in mitral insufficiency if the mitral orifice is very large, or if the intraventricular pressure is low at the time of operation

Course and Prognosis.—Mitral insufficiency of moderate degree may remain stationary, and the patient may never develop cardiac symptoms However, over a period of years, progressive changes in the valve leaflets, or further shortening of the chordæ may aggravate the degree of insufficiency and produce more and more left auricular and left ventricular hypertrophy, and eventual left-sided heart failure. Once this happens, the increased pressure in the pulmonary circuit causes right ventricular and right auricular enlargement, and right-sided heart failure may eventually occur. Another common complication of even mild mitral insufficiency is the development of subacute bacterial endocarditis on an otherwise innocuous insufficient mitral valve. Auricular thrombosis and embolism are less common in mitral insufficiency than in mitral stenosis.

Treatment.—Uncomplicated mitral insufficiency requires no treatment However, I treat such patients as if they had potential heart failure I suggest that the patient guard against factors which might precipitate congestive heart failure (page 247) I place the patient on a salt-poor, not necessarily a low-sodium diet (page 248), and if the patient is overweight, on a low-caloric diet (page 250). Ordinary physical activity is not limited, but competitive sports are not allowed When dental extractions or other oral surgery is performed, I give penicillin prophylactically to prevent subacute bacterial endocarditis (page 508). If heart failure occurs, it is treated in the usual way (page 248).

The surgical treatment of mitral insufficiency by using a pedicle tube graft of pericardium and passing one end through the left ventricle to form a mitral valve prosthesis must still be considered experimental.

Mitral Stenosis.—Mitral stenosis occurs because of fusion of the valve leaflets at the commissures. When the stenosis is marked, the fused, thickened and stiff leaflets show a small slit-like opening which resembles a buttonhole or a fish mouth, and which may be so small that it may not admit the tip of the small finger. On occasion, fusion of the leaflets and chordæ with each other occurs to such an extent that the valve assumes a funnel shape, the apex of the funnel pointing into the left ventricular cavity.

Mitral stenosis produces left auricular and right ventricular dilatation and hypertrophy in the following way: Because of the stenosis, the flow of blood from the left auricle into the left ventricle is retarded. The left auricle therefore dilates to accommodate the excess blood, and left auricular pressure rises. The dilatation of the auricle may reach such a degree that an aneurismal-like giant left auricle, holding more than a liter of blood may develop.

When a giant left auricle is present, one can assume that there is also a marked degree of mitral insufficiency as well as mitral stenosis.

Because of the increased left auricular pressure, the pressure in the pulmonary circulation rises, and over a period of time, marked sclerotic changes develop in the pulmonary arterioles. Because the right ventricle has to work against a higher resistance, right ventricular and eventually right auricular dilatation and hypertrophy occur. The left ventricle does not enlarge, and if the stenosis is very marked, the left ventricle may undergo atrophy because so little blood enters the left ventricle.

A new factor, the pleurohilar veins, has recently been described as one of the causes of the pulmonary congestion seen in mitral stenosis The pleurohilar vessels supply and drain the hilar structures and the subpleural area They communicate with the pulmonary venous system, but instead of emptying into the left auricle, they drain into the azygos vein and thus into the right auricle. As a result, the venous return to the right side of the heart is increased.

Symptoms.—Many cases of mitral stenosis present no symptoms. However, cough, hoarseness, and dysphagia may occur because of the enlargement of the heart Bronchial irritation and cough may develop when the left main bronchus is lifted up by the large left auricle (page 189). Posterior displacement of the esophagus by the left auricle may produce dysphagia. Hoarseness occurs from pressure on the left recurrent laryngeal nerve. This is not due to the left auricle, but is due to pressure on the nerve by a dilated left pulmonary artery

Hemoptysis, ranging from blood-streaked sputum to massive hemorrhage may occur because of the marked pulmonary congestion that is present A dull precordial ache is common, but anginal attacks due to mitral stenosis are very rare Menstrual disturbances have been described in women.

Signs.—Mild cyanosis, especially a malar flush (page 134) is common. The pulse may be small in amplitude, due to the small left ventricular output

Inspection of the chest may reveal a prominence of the precordium, and outward and upward displacement of the left nipple, due to the large right ventricle (page 153). The apical impulse may not be forceful and is displaced horizontally and to the left.

On palpation, a forceful systolic impulse is noted at the left lower border of the sternum, also due to right ventricular hypertrophy (page 154). A diastolic or presystolic thrill may be noted at the apex in association with a diastolic or presystolic apical murmur. Palpation of the apex may also reveal an abrupt systolic shock corresponding to the sharp first sound, and at the pulmonary area, an abrupt diastolic shock, corresponding to the accentuated pulmonary second sound is occasionally felt.

Percussion shows the area of cardiac dullness to be enlarged to the right of the sternum, in the fourth and fifth intercostal spaces, and to the left, especially at the level of the third and fourth intercostal spaces. The area of *absolute cardiac flatness* is also increased (page 156, and Fig 39, page 156)

Auscultation reveals characteristic findings at the apex, namely, a sharp first sound (page 157), the opening snap of the mitral valve (page 159), which may not always be present, and a soft, rumbling diastolic murmur, with or without a presystolic component, transmitted toward the axilla If auricular fibrillation is present, the diastolic murmur is heard without a presystolic apical murmur (page 167) The pulmonary second sound is accentuated and may be split, and a Graham Steell murmur (page 164) is common, with or without a pulmonary systolic murmur.

Fluoroscopic and X-Ray Examination (Figs. 42, *B*, page 185, 44, page 188, 45, page 189) —In the *P-A* position, the shape of the heart is very characteristic The aortic knob is small, the pulmonary artery segment enlarged, as are the secondary pulmonary branches, and a large left auricle can often be seen extending to the left border of the heart just below the pulmonary artery segment, and to the right border of the heart, forming a double contour within the right auricular shadow Figs 42, *B*, 45)

In the R A O position, the right ventricle is enlarged, the pulmonary artery dilated, and characteristic backward displacement of the esophagus by the left auricle is present (page 188)

In the L A O position, the large left auricle may elevate and compress the left main bronchus (page 189) Enlargement of the right ventricle is present, and the right auricle may appear enlarged.

Electrocardiogram —Broad and notched *P* waves may be present in standard leads I, II, and in leads *aVL*, *aVR* or *aVF*, and precordial leads $V_{1,2}$ may show large biphasic *P* waves, due to the auricular hypertrophy However, auricular fibrillation is often present.

The *QRS* complexes usually do not show signs of right ventricular hypertrophy, but rather evidence of a vertical heart with marked clockwise rotation (page 86)

Diagnosis —The two most characteristic signs of mitral stenosis are the presence of a rumbling apical mid-diastolic murmur, with or without a presystolic component, in the absence of signs of marked left ventricular hypertrophy or cardiac dilatation, and roentgenologic evidence of enlargement of the left auricle. However, even if the diastolic murmur is inaudible, the presence of a sharp apical first sound and an opening snap of the mitral valve is presumptive evidence of mitral stenosis

Difficulties in diagnosis are encountered when an apical diastolic murmur due to dilatation of the left ventricle is present, as in cases of aortic insuffi-

ciency, cardiac decompensation, acute carditis, and severe anemias, especially sickle cell anemia. However, in such cases, physical signs of aortic insufficiency, heart failure, or anemia are present, and adjuvant signs of mitral stenosis, such as the opening snap of the mitral valve or auricular fibrillation, are absent. Rarely a pedunculated tumor of the left auricle can simulate mitral stenosis (page 737). In addition, one should not forget that mitral stenosis can occur in association with an interauricular septal defect, producing the Lutembacher syndrome (page 405). It has been stated that in the presence of pulmonary tuberculosis, mitral stenosis is rare. However, the two conditions can be present simultaneously.

Course and Prognosis.—When the stenosis is marked, signs of left-sided heart failure appear early in adult life, along with auricular fibrillation, and eventual right-sided failure. Death may occur from heart failure or from embolic complications.

Embolic complications are very common. They may occur in the following ways:

1. With the great dilatation of the left auricle, marked stagnation of blood occurs, and thrombi form, especially in the auricular appendages. This is facilitated by the presence of auricular fibrillation, because the fibrillating auricles do not contract effectively, and remain more or less in a state of diastole. However, thrombi and emboli may occur even when sinus rhythm is present. The thrombi can also form in the absence of stagnation, over areas of endocardium injured by the rheumatic inflammation. Fragments from an auricular thrombus may embolize to the brain, producing hemiplegia and aphasia; to the intestinal viscera, producing mesenteric embolism and even gangrene of the gut; to the kidneys, resulting in pain and hematuria (page 668); to the spleen (page 668); to the extremities, resulting in acute pain, pallor, coldness, loss of pulsation and even gangrene of a portion of the limb (page 668), and to many other organs.

2. Infarction of the lung may result from thrombi in the right auricle. However, a very common source of pulmonary infarcts, especially in bedridden patients, is the veins of the lower extremities. In such cases, the pulmonary embolism may merely aggravate the dyspnea and pulmonary congestion, rather than producing chest pain and hemoptysis, and is frequently mistaken for an exacerbation of heart failure, because the veins of the lower extremities may not show signs of active inflammation.[1]

3. An unusual thrombotic complication occurs from a ball thrombus (ball-valve thrombus) in the left auricle. In such a case, either a pedunculated thrombus or a ball-like thrombus, floating free in the left auricle, more or less occludes the mitral orifice, resulting in either sudden death, or a characteristic clinical picture of shock with intense cyanosis, symmetrical cadaveric coldness of all four extremities with absent pulsations, and with a cadaveric cyanosis of the nose and ears, and even gangrene of some of these regions. Syncope or a convulsive seizure may occur because of cerebral anoxia. This clinical picture is not pathognomonic of a ball-valve thrombus, and may occur in its absence when intense peripheral vasoconstriction occurs after shock, as in the course of acute myocardial infarction, or heart failure. It can also occur in cases of pedunculated left auricular tumors (page 737).

When a ball valve thrombus is very large, it can cause symptoms by acting as a space occupying mass and preventing an adequate volume of blood from entering the left auricle during diastole It can also occlude some of the pulmonary veins and in this way decrease the amount of blood entering the left auricle.

In rare cases, a ball valve thrombus of the right auricle occurs This is difficult to diagnose Sudden attacks of air hunger may occur, associated with marked distention of the neck veins, and cyanosis

A complication, such as subacute bacterial endocarditis, is rare in cases of long-established mitral stenosis, especially if auricular fibrillation is present This is probably due to the fact that by the time auricular fibrillation develops, the intense scarring of the valve and loss of its blood vessels make implantation of the streptococcus viridans difficult Essential hypertension frequently develops in middle-aged patients with mitral stenosis. This has been considered by some as a good prognostic sign, possibly because the left ventricle tends to dilate and to diminish the degree of mitral stenosis

Treatment —Treatment is similar to that of mitral insufficiency, page 525 However, the danger of heart failure is much greater in mitral stenosis than in mitral insufficiency.

The treatment of pulmonary or systemic embolization and infarction complicating mitral stenosis and auricular fibrillation is difficult because the source of the thrombi is either a thrombus in the left or right auricle or both Surgical resection of the auricular appendage to prevent further thrombus formation and so to prevent embolization must still be considered experimental Two other therapeutic measures can be used The patient can be placed on long-term anticoagulant therapy with Dicumarol (page 618) to prevent or decrease thrombus formation. In some cases, restoration of the auricular fibrillation to sinus rhythm by means of quinidine (page 346) also will stop embolization. Actually, there is no satisfactory solution to this problem as yet

The Surgical Treatment of Mitral Stenosis —Attempts to alleviate the mitral stenosis surgically have become popular in the past few years Several methods of enlarging the stenosed valve opening have been used. The more commonly used methods include.

1. Simple digital dilatation of the stenotic orifice (finger fracture valvuloplasty) This is usually effective where the valve cusps are fused However, in the rarer funnel type of mitral stenosis where the chordæ tendineæ are also affected (page 482), this may not be sufficient to relieve the obstruction

2. Valvuloplasty. Harken has used the term, valvuloplasty, to describe his procedure of resecting a wedge-shaped portion of the valve ring at the commissures.

3 Commissurotomy. This is a term suggested by Bailey and his colleagues to describe the procedure in which the valve commissure is cut apart with a specially designed knife attached to the gloved finger and introduced through the left auricular appendage.

Indications for Mitral Valve Surgery.—Patients with mitral stenosis who are being considered for mitral valve surgery can be divided into four groups, *viz* :

Group I.—These patients have a benign present course. There are few if any symptoms and minimal signs of pulmonary hypertension.

Group II.—These patients suffer with moderate dyspnea on exertion, or rare attacks of acute dyspnea or other pulmonary symptoms produced by some extrinsic cause, such as unusual exertion, or severe infection. The symptoms are not progressive. Rarely, minimal ankle edema may be present, but signs of marked right-sided heart failure are absent.

Group III.—These patients have a progressive disability. There may be increasing dyspnea on exertion. Attacks of hemoptysis, chest pain and pulmonary edema are easily provoked. They may suffer from palpitation, tachycardia and pain over the liver on exertion. At any time, they may become worse and show signs of *group* IV or may die in an acute attack of pulmonary edema or from peripheral or pulmonary infarction. Their life expectancy under medical therapy is hazardous.

Group IV.—This is a terminal group. These patients are completely incapacitated. Severe right-sided heart failure is usually present with chronically elevated venous pressure, marked engorgement of the liver and a marked tendency to pulmonary congestion. The pulmonary disability may or may not be greater than in *group* III. There is often poor liver function, even ascites, evidence of decreased peripheral blood flow, and many patients have had emboli. Most of them have auricular fibrillation.

The surgeons believe that surgery should not be done in *group* I and II cases, and that *group* III patients are the ideal candidates for surgery, with an operative mortality of less than 10 per cent. The operative mortality in *group* IV is about 40 per cent, but this is not considered a contraindication to operation.

The most important criterion for mitral valve surgery is the presence of pulmonary hypertension. This can usually be determined by the presence of the following symptoms and signs:

1. Hemoptysis and nocturnal dyspnea. However, these symptoms can occur in patients who have only mild or moderate pulmonary hypertension and are not of much value in determining the degree of pulmonary hypertension.

2. Prominent auricular venous waves in the neck veins. This is an important clinical sign of pulmonary hypertension in patients who have sinus rhythm.

3. A forceful systolic pulsation to the left of the sternum at about the level of the fourth intercostal space. This is also a good sign of both right ventricular hypertrophy and pulmonary hypertension.

4. A palpable second heart sound is a good sign of moderate or severe pulmonary hypertension.

5. A loud and split second heart sound is not a reliable sign of marked pulmonary hypertension, because it may occur in the early stages of pulmonary hypertension.

6. A Graham Steele murmur, however, is a good sign of pulmonary hypertension. The murmur of aortic insufficiency should not be mistaken for a Graham Steele murmur.

7. Electrocardiographic evidence of right ventricular hypertrophy, such as a tall R in lead V_1 (page 211) is also evidence of pulmonary hypertension

8. Fluoroscopic and x-ray examination will reveal increased or marked prominence of the pulmonary arteries with marked pulmonary artery pulsations.

The shape of the pulmonary artery and its branches is related to the severity of the pulmonary hypertension. When pulmonary artery pressure is less than 40 mm. Hg, the pulmonary artery and its branches may appear normal on the x-ray film. When pulmonary hypertension is present and the pulmonary artery pressure is between 40 to 70 mm. Hg, the main branches of the pulmonary artery are enlarged and the distal branches are narrow, irregular and tortuous, especially in the lung bases, close to the heart When the pulmonary artery pressure exceeds 70 mm Hg, these changes are widespread.

The following conditions are contraindications to the operation:

1 Active rheumatic carditis.

2 Severe aortic valvular disease (stenosis or insufficiency) sufficient to produce peripheral signs of aortic insufficiency or of a definite enlargement of the left ventricle

3. Mitral insufficiency This is a relative contraindication, because the operation can be successful in the presence of a mild degree of mitral insufficiency The degree of mitral insufficiency is difficult to determine clinically (see page 524).

4 Subacute bacterial endocarditis The operation can be done after six to eight weeks of antibiotic therapy. However, it is better to wait six or more months

5 Auricular fibrillation itself or a history of peripheral embolization is not a contraindication to operation. Extensive valvular calcification is also not a contraindication

6 Advanced age is a relative contraindication Patients between the ages of thirty and forty years do best. After fifty years, the incidence of postoperative complications tends to increase

7. Organic tricuspid stenosis makes the operation more dangerous. This is a difficult diagnosis to make. Catheterization findings of a higher diastolic pressure in the right auricle than in the right ventricle indicate tricuspid stenosis

If mitral and tricuspid stenosis are present and the mitral stenosis is relieved by surgery, the signs of the tricuspid stenosis may become much worse because the subsequent increase in cardiac output resulting from the operation requires a greater pressure in the right auricle and the systemic veins to force the blood through the tricuspid valve. In such cases, it may be necessary to operate on the tricuspid valve immediately after the mitral valve orifice is enlarged

8 Associated diseases, such as generalized arteriosclerosis, hypertensive heart disease, asthma or other debilitating conditions also increase the risk of the operation

9. If heart failure is so intractable that the patient cannot be adequately compensated and prepared for operation, the operation should not be performed.

10 Pregnancy is also a relative contraindication to the operation.

11. Recent pulmonary infarction is a relative contraindication. However, the operation can be performed after two weeks of anticoagulant therapy

Preoperative Care.—Cardiac compensation should be restored as much as possible by means of a low-sodium diet, diuretics and digitalis. All patients, regardless of whether they are in sinus rhythm or fibrillating, should be digitalized before the operation

Operative Complications —During the operation the following complications may occur: cardiac standstill, cardiac arrhythmias, such as auricular premature beats, auricular tachycardia, nodal rhythm, ventricular premature beats, ventricular tachycardia, ventricular fibrillation, hypotension, hemorrhage, rupture of the left auricle, or thromboembolic phenomena from the left auricle, particularly cerebral embolism.

Premature beats and tachycardias occurring during the operation can usually be controlled with intravenous pronestyl. Abnormal slow rhythms respond to 0 6 mg atropine intravenously. The treatment of cardiac arrest and ventricular fibrillation is described on page 763.

Postoperative Complications —The most serious postoperative complication of mitral valve surgery is a reactivation of acute rheumatic fever. This may occur in almost twenty-five per cent of the cases operated upon Other complications which may occur postoperatively are hemiplegia or peripheral embolic phenomena, auricular fibrillation which often occurs one to three days postoperatively, progressive enlargement of the heart with or without signs of further heart failure, or signs of frank mitral insufficiency. In rare cases, the valve cusps may fuse again after one or two years

The characteristic physical signs and murmurs of mitral stenosis usually persist after the operation However, a significant decrease in the apical diastolic murmur is a good clinical sign. No decrease in the apical diastolic murmur or the development of a postoperative apical systolic murmur of grade 3 intensity or greater, generally indicates a poor post-operative result.

Although there is much enthusiasm for mitral valve surgery, my experiences to date lead me to restate my belief that the primary treatment of mitral stenosis is still medical

Mitral Insufficiency and Stenosis.—As I mentioned above, most cases of rheumatic heart disease affecting the mitral valve show some degree of stenosis and insufficiency Some degree of left ventricular enlargement is present, and on auscultation, a systolic apical murmur appears along with the diastolic murmur. The clinical course and prognosis depend on whether predominant stenosis or insufficiency is present

Combined Mitral and Aortic Lesions.—See page 536.

RHEUMATIC LESIONS OF THE AORTIC VALVE

Just as with mitral valve lesions, aortic stenosis or aortic insufficiency may exist independently or together. Occasionally, rheumatic involvement of the aortic valve produces an acquired bicuspid aortic valve. (The differentiation of an acquired from a congenital aortic valve is often very difficult, and some pathologists believe that a bicuspid aortic valve should be considered acquired unless other congenital lesions are present)

Aortic Stenosis.—Aortic stenosis results from fusion of the aortic valve *leaflets at the commissures.* Calcific changes frequently appear over a period of years, and the annular ring as well as the leaflets may be calcified Masses of calcium may develop on the leaflets and may project into the sinuses of Valsalva, and even interfere with the coronary artery flow.

The stenosed valvular orifice offers resistance to the outflow of blood from the left ventricle, which hypertrophies to maintain an adequate cardiac output. According to Starling's Law (page 231), the hypertrophy should be associated with dilatation but the process of progressive aortic stenosis is so slow that at autopsy the heart often shows marked concentric hypertrophy, that is, hypertrophy with little or no dilatation The forceful propulsion of blood towards the stenosed valve may produce endocardial pockets on the wall of the left ventricle, below the valve. These endocardial pockets consist of thickened fibrous mural endocardium, and may be discrete or multiple The openings of the pockets are directed toward the apex of the heart Similar endocardial pockets occur below a stenosed mitral valve

Symptoms —Patients with aortic stenosis may have no symptoms However, some patients complain of vertigo, attacks of syncope, and even sudden death may occur with moderate or mild exertion The cause of this is obscure, but it is usually not due to carotid sinus sensitivity. Vague precordial pain is common, and true anginal attacks may occur.

Signs.—Because of the slow ejection of blood from the left ventricle, the systolic pressure may be low with a small pulse pressure, for example, 110/90, and a slowly rising plateau pulse (page 140) may be palpated However, the pulse pressure may be normal, and hypertension may even be present The heart rate is often slow, between 60 and 70, but this is not a constant finding

Because the ejection of blood sets the stenosed aortic valve in vibration, a rough systolic thrill may appear in the aortic valve area in association with a loud, harsh systolic murmur which may replace the first heart sound and which may be transmitted to the neck vessels and over the thorax (page 161) The aortic second sound is faint or absent.

Recent autopsy studies have shown that aortic stenosis may exist even when these signs are absent. It has been found, for example, that aortic stenosis can be present without either a systolic thrill or murmur at the aortic area, and even when present, the murmur may be transmitted to the neck vessels in slightly less than one-half of those cases in whom it was heard. Basal diastolic murmurs may also appear in one-third of patients with pure aortic stenosis In addition, apical systolic and even diastolic murmurs may appear These unusual murmurs may be caused by transient cardiac dilatation and functional aortic insufficiency. Some cases may only show an apical systolic murmur. The aortic second sound may even be loud in spite of the aortic stenosis This is probably due to transmission of the pulmonary second sound to the right of the sternum

Fluoroscopic and X-Ray Examination —Moderate enlargement of the left ventricle is usually present. Occasionally the left ventricular contour appears normal because the hypertrophy is concentric Calcification of the aortic valve is occasionally seen (page 196).

Electrocardiogram —The tracing may be normal, or may show signs of left ventricular hypertrophy or strain or both (page 210).

Diagnosis.—The physician who refuses to make a diagnosis of aortic stenosis, unless the aortic systolic thrill and murmur are present along with an absent aortic second sound, will miss many cases of aortic stenosis. *Actually, the presence of a loud, harsh aortic systolic murmur in a patient* without aortic dilatation or hypertension is itself sufficient to make the diagnosis. When an aortic diastolic murmur is present in addition to the systolic murmur, the differentiation of uncomplicated aortic stenosis from aortic stenosis and insufficiency may be impossible unless the peripheral signs of aortic insufficiency are also present. The differentiation of other conditions producing an aortic systolic murmur is described on page 162. When an aortic systolic murmur is transmitted to the apex, an erroneous diagnosis of mitral insufficiency may be made. However, unlike the murmur of mitral insufficiency, the aortic systolic murmur is not transmitted beyond the apex to the axilla.

Course and Prognosis.—Patients with uncomplicated aortic stenosis may live to old age, dying of an unrelated condition. However, in many patients, left-sided heart failure eventually occurs. Subacute bacterial endo-*carditis, engrafted on the aortic valve is common. Syncopal attacks* and sudden, unexplained death has already been mentioned. Patients with aortic stenosis who suffer from anginal attacks may die during an attack In such cases, autopsy may disclose acute myocardial infarction, even though the coronary arteries are patent. Auricular fibrillation is infrequent unless coincidental mitral involvement is also present.

Treatment —The general measures described for mitral insufficiency can be used (page 525). There is no effective treatment for the syncopal attacks these patients may have. The anginal attacks are relieved by nitrites (page 304) If heart failure occurs, it is treated in the usual way (page 247).

Aortic Insufficiency.—Because of thickening, rigidity and retraction of the aortic leaflets, the valve may become insufficient, and blood regurgitates through it from the aorta into the left ventricle during diastole. This causes dilatation of the left ventricle and hypertrophy, because the work of the left ventricle is increased proportionately to the amount of blood that regurgitates. Endocardial pockets may appear in the wall of the left ventricle, due to the impact of the regurgitating column of blood on the ventricular wall. The openings of these pockets point toward the insufficient aortic valve (Similar endocardial pockets appear in the left ventricle in *cases of mitral insufficiency.*)

Symptoms.—Many patients with aortic insufficiency have no symptoms Others complain of dull precordial pain, or of very severe anginal attacks even at rest. The anginal attacks may be due to myocardial anoxia resulting from the low diastolic blood pressure present, because, as Anrep has shown, one of the primary factors affecting coronary artery *blood flow* is the average pressure in the aorta during diastole. Occasionally patients complain of palpitation, due to the forceful heart beat. Vertigo and syncopal attacks may also occur as in cases of aortic stenosis.

Signs.—Because of the regurgitation of blood from the aorta into the left ventricle during diastole, the diastolic blood pressure drops to 30 or 40 mm,

and may even fall to 0 mm. This produces characteristic peripheral signs, such as the collapsing or Corrigan pulse (page 140) and Duroziez's sign (page 144). Capillary pulsation (page 140) may also be present.

Marked pulsation of the peripheral arteries may cause shaking of the head, synchronous with systole (de Musset's sign), and even the retinal arteries can be seen to pulsate on ophthalmoscopic examination

Along with the low diastolic pressure, there is usually systolic hypertension, and the systolic pressure may rise above 200 mm. In association with this, the pressure in the lower extremities rises greatly and may even be 100 mm. or more than the systolic pressure in the arms (Hill's sign). However, one should remember that even normally, the blood pressure in the lower extremities is somewhat greater than in the arms (page 32).

Examination of the thorax reveals the following: On inspection, marked pulsation of the neck vessels and in the suprasternal notch is visible. The apical impulse can often be seen displaced to the left and downward, beating forcibly.

On palpation, the apical impulse lifts the palpating hand forcibly and is broad and very resistant, due to the left ventricular hypertrophy, and may be felt in the anterior axillary line even in the sixth intercostal space A diastolic thrill at the aortic area is rarely palpated.

Percussion reveals the heart to be enlarged principally to the left

On auscultation, a characteristic blowing diastolic murmur, due to the regurgitating blood, is heard best along the left sternal border, at the level of the second or third intercostal space, transmitted to the aortic area and downward toward the apex (page 162). A systolic murmur may also be present This is due to the forceful ejection of blood from the left ventricle during systole, and is not due to aortic stenosis. Occasionally an apical presystolic or diastolic murmur (the Austin Flint murmur, page 168) is heard

Fluoroscopic and X-Ray Examination—Marked rounding and elongation of the left ventricle (page 181), with some dilatation of the aorta (page 191) is present. However, when the aortic insufficiency is minimal, the heart may be only slightly enlarged.

Electrocardiogram.—In the early stages of aortic insufficiency, the tracing may be normal Later, signs of left ventricular hypertrophy or strain or both appear (page 210) The heart is usually horizontal

Diagnosis.—When marked left ventricular enlargement is present, along with a soft, blowing, diastolic murmur, with or without a systolic murmur along the left sternal border, and the pulse pressure is large and the diastolic pressure low, the diagnosis of aortic insufficiency is simple. However the differentiation of uncomplicated aortic insufficiency from aortic insufficiency with stenosis may be difficult if not impossible if the double murmur is present and the diastolic pressure only moderately low, for example, 60 mm. Similarly, the differentiation of uncomplicated rheumatic aortic insufficiency from syphilitic aortic insufficiency may be difficult (page 545). Uncomplicated aortic stenosis may also exist with a double aortic murmur, but here the peripheral signs of aortic insufficiency, such as a collapsing pulse, Duroziez's sign, *etc*, are absent.

Functional aortic insufficiency, with all the characteristic physical signs of organic aortic insufficiency can also occur in dissecting aneurism of the aorta (page 659) and in *dynamic dilatation of the aorta*. In this condition, there is a functional dilatation of the ascending aorta and the aortic valve. It occurs in patients with hypertensive cardiovascular disease, glomerular nephritis, in severe anemias, in hyperthyroidism, and may even occur in patients with rheumatic heart disease. On physical examination, marked *suprasternal pulsations may be visible, and on fluoroscopic and x-ray examination*, the aorta appears dilated and pulsates vigorously. Auscultation reveals the characteristic murmurs of aortic insufficiency, and the wide pulse pressure and other peripheral signs of organic aortic insufficiency may be present. However, at autopsy, in such cases, a normal aortic valve is found, and the aorta may actually be hypoplastic. Dynamic dilatation of the aorta can sometimes be suspected if the signs of aortic insufficiency appear only during a time when the heart is overactive, or the patient is in heart failure, the signs disappearing when the heart rate slows, or when cardiac compensation returns.

Course and Prognosis.—Aortic insufficiency is not in itself a contraindication to long life. However, when it is marked, anginal attacks and heart failure—first left-sided and then right-sided—occur early in adult life, with death a few years later. Subacute bacterial endocarditis is also a common complication.

Treatment.—This is the same as for aortic stenosis, page 535

Aortic Insufficiency and Stenosis.—Many patients with chronic rheumatic heart disease show signs of both aortic insufficiency and stenosis. In such cases, the characteristic blowing diastolic murmur of aortic insufficiency is present, but often very faint, and the peripheral signs of aortic insufficiency are usually absent.

The *systolic murmur is harsh and an aortic systolic thrill may be present*. The aortic stenosis tends to ameliorate the effects of the aortic insufficiency by decreasing the amount of blood that regurgitates. However, this is offset in some measure by the fact that the work of the left ventricle is increased in propelling blood through the stenosed valve.

Combined Aortic and Mitral Lesions.—Various combinations of aortic and mitral valvular lesions are common. The signs depend on the degree of mitral or aortic insufficiency and stenosis It is often difficult to determine whether one valve or multiple valves are involved. For example, in the presence of aortic insufficiency, an apical presystolic murmur may be due to concomitant organic mitral stenosis or may be an Austin Flint murmur due to functional mitral stenosis. *X*-ray signs of marked left auricular enlargement, or the presence of a sharp, snapping first apical sound, or of a diastolic or presystolic apical thrill will favor an organic *mitral stenosis*. Similarly, the diastolic murmur of aortic insufficiency may be transmitted to the apex. In such a case, the apical murmur has the same characteristics as the murmur of the base, indicating that it is transmitted.

When mitral stenosis and aortic insufficiency or stenosis are present, the mitral stenosis causes a decreased filling of the left ventricle, and diminishes the intensity of the physical signs of the aortic insufficiency. Mitral insufficiency on the other hand, complicating aortic insufficiency, *tends to ag-*

gravate the condition of the patient by increasing the work of the left ventricle.

RHEUMATIC LESIONS OF THE TRICUSPID VALVE

Tricuspid valve lesions are infrequent compared to the incidence of mitral and aortic lesions, and when they do appear, are almost always associated with either severe mitral or aortic lesions or both.

Tricuspid Insufficiency.—Organic tricuspid insufficiency usually occurs in combination with tricuspid stenosis. Functional tricuspid insufficiency is much more common. There may be no signs of the tricuspid insufficiency or systolic pulsation of the liver and neck veins, *etc.*, may be present (page 149).

Tricuspid Stenosis.—Stenosis of the tricuspid valve causes obstruction to the flow of blood from the right auricle to the right ventricle, and therefore produces marked enlargement of the right auricle Since less blood flows into the right ventricle, the right ventricle may actually atrophy. However, mitral stenosis with right ventricular hypertrophy is usually present The occurrence of tricuspid stenosis in such a case tends to decrease the work of the right ventricle. The decreased filling of the right ventricle also results in a decreased pulmonary blood flow, the blood being dammed back in the peripheral veins.

Symptoms.—Patients with tricuspid stenosis may show no symptoms due to the stenosis, but, most of the patients suffer from long-standing heart failure and have exertional dyspnea. However, because of the relative lack of pulmonary congestion, orthopnea and cough may be absent even when signs of marked right-sided failure, such as edema, marked distention of the neck veins, enlargement of the liver, even ascites, are present

Signs.—The signs of tricuspid stenosis are related to the chronic right-sided heart failure present, and to the large right auricle and right ventricle usually present. A combination of pallor, cyanosis and jaundice may occur. The pallor is due to secondary anemia. (However, secondary polycythemia may appear) The cyanosis is peripheral in type and is due to stagnation as a result of the right-sided failure The jaundice is due to intense chronic liver congestion The neck veins are markedly engorged, and may or may not show pulsations. Many patients show auricular fibrillation due to concomitant mitral stenosis

Physical examination of the chest often reveals the signs of mitral stenosis (page 526). Percussion of the chest usually shows flatness beyond the right of the sternum, due to the large right auricle. On auscultation, the vibrations set up by the flow of blood through the stenosed tricuspid valve during diastole may produce a rumbling diastolic murmur in the tricuspid valve area (region of the xiphoid process) and to the right of the sternum, near the right nipple However, a murmur, if heard here, may be transmitted from the mitral valve area (see page 165). A systolic murmur, accentuated by holding the breath after a deep inspiration, may occur in the tricuspid area because of concomitant tricuspid insufficiency (page 165)

Marked enlargement of the liver is usually present, and there may be ascites The liver sometimes shows a strong presystolic pulsation if sinus rhythm is present, transmitted from the strongly contracting right auricle.

Fluoroscopic and X-Ray Examination.—Marked enlargement of the right auricle is present (page 191). The right ventricle is also enlarged The aortic knob is small and not prominent unless an aortic lesion is also present. Left auricular enlargement, due to concomitant mitral stenosis, is often present. Pulmonary congestion may be minimal.

Electrocardiogram.—Signs of a vertical heart with marked clockwise rotation are usually present. Large, broad *P* waves, and very large *P* waves in leads $V_{1\ 2}$ due to right auricular hypertrophy may be present. The precordial leads may also show signs of right ventricular hypertrophy (page 211). Auricular fibrillation is often present.

Laboratory Tests.—The venous pressure is high, and the arm-to-lung circulation time prolonged.

Diagnosis.—In the presence of chronic rheumatic heart disease, signs of marked right-sided heart failure with a large liver, distended neck veins, and minimal signs of left-sided heart failure with little or no orthopnea, should make one suspect the presence of a tricuspid lesion. The presence of pallor, cyanosis and jaundice, or the presence of a mid-diastolic murmur at the xiphoid process, is not pathognomonic of a tricuspid lesion nor are any of the physical or laboratory signs described above

Tricuspid insufficiency or stenosis can simulate chronic constrictive pericarditis because in both conditions signs of severe right-sided failure and minimal left-sided failure are present, the liver is large, ascites may be present, the neck veins are congested and the venous pressure is very high, and even a diffuse systolic depression over the precordium with a diastolic rebound may appear. Points of differentiation are the very large heart seen on roentgenologic examination in tricuspid lesions, whereas the heart in constrictive pericarditis is usually small or only slightly enlarged (However, marked enlargement of the heart can also occur in constrictive pericarditis.) Systolic pulsation of the liver or neck veins occurs in tricuspid lesions but not in constrictive pericarditis. Valvular murmurs are present in tricuspid stenosis and not in constrictive pericarditis. The electrocardiogram is also helpful because in tricuspid lesions, signs of auricular and right ventricular hypertrophy are often present, whereas in constrictive pericarditis, abnormal *T* waves appear (page 632). *X*-ray examination may show calcification of the pericardium. This is suggestive but not pathognomonic of constrictive pericarditis, because calcification may be present without constrictive pericarditis, and constrictive pericarditis may be present without calcification.

Course and Prognosis.—Patients with tricuspid valvular lesions usually develop congestive heart failure early in adult life. However, the presence of the tricuspid stenosis and the peripheral venous congestion act to decrease the work of the heart by preventing overloading of the circulation, just as occurs in cases of constrictive pericarditis, so that the patient may live many years in semi-invalidism However, death eventually occurs either from a recurrence of rheumatic activity, from multiple pulmonary emboli, originating from a thrombus in the right auricle, or from congestive heart failure.

Treatment.—There is no specific treatment for tricuspid valve lesions, and the general measures described for mitral stenosis (page 529) can be

used. Surgical procedures, such as tricuspid valvulectomy, or ligation of the inferior vena cava, to decrease the blood in the right side of the heart, *etc.*, must still be considered experimental.

RHEUMATIC LESIONS OF THE PULMONARY VALVE

Although microscopic or minimal lesions of the pulmonary valve are not uncommon, organic pulmonary insufficiency is rare, and pulmonary stenosis of any degree does not occur. Functional pulmonary insufficiency, due to pulmonary artery dilatation is common, and results in the Graham Steell murmur (page 164). There is no way of differentiating functional from organic pulmonary insufficiency. The blood regurgitating into the right ventricle increases the work of the right ventricle, but is relatively unimportant in causing right ventricular enlargement compared to the mitral stenosis which is usually present.

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Chapter 35

SYPHILITIC HEART DISEASE

CARDIOVASCULAR syphilis is essentially a disease of the arteries, especially of the aorta, and the myocardium is only rarely involved. Therefore the following discussion shall center chiefly on syphilitic aortitis and its complications

Pathology.—The primary lesion in the aorta is probably an obliterative arteritis of the vasa vasorum of the aortic adventitia. The media, which is nourished by the vasa vasorum is secondarily affected because of the narrowing or occlusion of the vasa, and necrosis and destruction of the muscle fibers and elastic tissue of the media, with subsequent scar formation occur (productive mesaortitis). Even calcification of the media may result. Some inflammatory reaction of the media also probably occurs because collections of small lymphocytes and plasma cells can be found, and rarely gummata may appear in the media

The destruction of the elastic fibers of the media produces flabbiness of the muscle wall and causes dilatation of the aorta, which may lead to the formation of aneurisms However, fibrous thickening of the intima occurs in the form of bluish-gray, porcelain-like plaques which tend to strengthen the weakened intima. In addition, the scar process in the media causes the intima to wrinkle with the formation of longitudinal and radial grooves, giving the intima the wrinkled appearance of the bark of a tree (tree-barking)

When syphilitic aortitis extends into the aortic valve, the destruction of the elastic fibers of media at the level of the aortic ring allows the aorta to widen at this level, and the commissural spaces between the valve leaflets widen and produce aortic insufficiency. In addition, the inflammatory process spreads into the aortic leaflets which become thickened and later fibrosed and shrunken, thus aggravating the aortic insufficiency. *Eversion of the valve leaflets may also occur, and they may become pressed* against the aortic wall and adherent to the sinuses of Valsalva. Thus, aortic stenosis cannot occur with syphilis. However, the presence of coincidental rheumatic aortic stenosis or calcification of the aortic leaflets (which is also probably rheumatic in origin in most cases) may produce aortic stenosis in the presence of cardiovascular syphilis The mitral or other valves are almost never involved by a syphilitic lesion Rarely the aortic valve is involved from extension of a gumma in the myocardium

The aortitis involves the ascending portion of the aorta most frequently. It only rarely extends below the line of attachment of the valve cusps into the sinuses of Valsalva, and almost never extends into the endocardium itself below the aortic valve. Superiorly, the syphilitic process often stops abruptly at the beginning of the descending aorta. However, the descending aorta or the abdominal aorta may be involved

Scar formation in the aorta may involve the mouths of the coronary arteries, producing narrowing or stenosis and even occlusion of the coronary arteries (coronary ostial stenosis). This is particularly marked when the coronary arteries do not originate normally from the sinuses of Valsalva but from the aortic wall above the sinuses Rarely syphilitic plaques occur at or just within the mouths of the coronary arteries, but the syphilitic process does not extend beyond the vessel mouth In spite of the fact that coronary artery stenosis or occlusion occur frequently with syphilitic aortitis, myocardial infarction is rare, though diffuse myocardial fibrosis may occur The reason for this is that the occlusive process is slow enough to allow an adequate collateral circulation to develop.

From a clinical point of view, cardiovascular syphilis can be considered under five headings: uncomplicated syphilitic aortitis, syphilitic aortic insufficiency; syphilitic aortitis with coronary ostial stenosis; syphilitic aneurisms of the aorta, and syphilitic myocarditis and gumma. Most cases of cardiovascular syphilis are due to acquired syphilis, and males are affected much more frequently than females Rarely, congenital syphilis produces aortic lesions in young people Symptoms of cardiovascular syphilis may occur as early as three years after infection. However, the diagnosis is usually first made ten, twenty, and even thirty years after the initial syphilitic lesion

UNCOMPLICATED SYPHILITIC AORTITIS

Symptoms —There are no symptoms of syphilitic aortitis, if it is uncomplicated by aortic insufficiency, coronary ostial stenosis, or aneurism of the aorta.

Signs —It has been stated that if the patient is under fifty years, and does not show evidence of either arteriosclerosis or hypertension, the presence of an accentuated aortic second sound of low pitch and of a so-called booming or tambour-like quality, is suspicious of uncomplicated syphilitic aortitis An additional sign is the presence of exaggerated aortic pulsations on fluoroscopy. Still further evidence is the presence of a faint systolic murmur at the second right intercostal space, and if dilatation of the aortic arch is present, the diagnosis is considered almost certain, especially if there is a history of syphilis or a positive serological reaction.

Fluoroscopic and X-Ray Examination.—Nonspecific dilatation of the aorta and exaggerated aortic pulsations may appear. More significant is calcification, especially linear streaks of calcification, in the ascending aorta However, even this is not pathognomonic of syphilitic aortitis and may occur with atherosclerosis of the aorta. The heart remains normal in size.

Angiocardiographic Examination.—Recently the following angiocardiographic signs of syphilitic aortitis have been described: dilatation of the mid-ascending aorta, so that the diameter is more than 38 mm., irregularity of the lumen of the ascending aorta; variations in thickness of the aortic wall; calcification of the ascending aorta; and tortuosity of the aorta.

Electrocardiogram.—The electrocardiogram is normal.

Laboratory Tests —A positive serological reaction occurs in up to 85 or 90 per cent of cases of cardiovascular syphilis, regardless of the site of the

lesion However, some investigators have obtained positive serological reactions in as high as 98 per cent of the cases of cardiovascular syphilis, using sensitive tests.

Diagnosis.—The signs of syphilitic aortitis described above are very common in patients with hypertensive cardiovascular disease. In hypertensive patients the booming aortic second sound may persist even if the blood pressure drops to normal for any reason. In addition, normal people with an overactive heart may show forceful pulsations of the aorta and an aortic systolic murmur (page 161). Even the presence of a positive serological reaction merely indicates the presence of syphilis, and not cardiovascular syphilis Furthermore, a false positive reaction may occur. For these reasons, I believe that it is almost impossible to make a clinical diagnosis of uncomplicated syphilitic aortitis, unless angiocardiographic studies are positive.

Course and Prognosis.—Even without treatment the patient may not develop any further cardiovascular complications, and the aortitis is often an incidental finding at autopsy.

Treatment.—See page 532.

SYPHILITIC AORTIC INSUFFICIENCY

Pathological Physiology.—The mechanism by which left ventricular hypertrophy occurs is similar in both syphilitic and rheumatic aortic insufficiency and is described on page 534.

Symptoms.—Syphilitic aortic insufficiency is usually symptomless. However, the low diastolic blood pressure which is present may disturb the coronary artery blood flow and may produce angina pectoris, just as in cases of rheumatic aortic insufficiency. However, in most patients with syphilitic aortic insufficiency who have anginal symptoms, there is usually some degree of coronary ostial stenosis, which further reduces the coronary blood flow, and may be responsible for the anginal symptoms.

Signs.—The physical signs and fluoroscopic and x-ray findings of syphilitic aortic insufficiency are similar to those of rheumatic aortic insufficiency (page 534) except that much more enlargement of the heart may occur in syphilitic aortic insufficiency than in rheumatic aortic insufficiency, because rheumatic aortic insufficiency is often associated with some degree of aortic stenosis which limits the volume of blood that can regurgitate.

The diastolic murmur of syphilitic aortic insufficiency is characteristically soft and blowing, usually heard best over the second right intercostal space, and is transmitted to the left of the sternum and along the left sternal border. It can sometimes be heard best by using a diaphragm type stethoscope chest piece and by having the patient sit and exhale. Occasionally the murmur is loud and musical, if the aortic valve leaflets are everted, and may sound like the buzzing of a saw. A diastolic thrill may also be palpable. Occasionally, the murmur is so loud that it can be heard at a distance from the patient. Rarely, it is only heard at the lower left sternal border. A loud aortic systolic murmur, due to the flow of blood through the dilated aorta, is usually also present (see also page 161).

Diagnosis.—The diagnosis is simple when the classical signs of aortic insufficiency are present. However, it may be difficult to differentiate syphilitic aortic insufficiency from rheumatic aortic insufficiency. Patients with rheumatic aortic insufficiency often give a history of rheumatic fever in childhood, and there may be signs of precordial bulging or displacement of the left nipple, due to the chronic rheumatic heart disease (page 153), or x-ray signs of enlargement of the left auricle, due to associated mitral stenosis may be present. On the other hand, patients with syphilitic aortic insufficiency often give a history of exposure or of a chancre; the serology is usually positive, and neurosyphilis is present in a high per cent of cases of cardiovascular syphilis and produces characteristic signs, such as inequality or irregularity of the pupils, the Argyll-Robertson pupil, loss or diminution of knee or ankle jerks, abnormal spinal fluid findings, *etc.* Other stigmata of syphilis such as bone or skin syphilides, may be present. (Incidentally, 50 to 70 per cent of patients with neurosyphilis have associated cardiovascular syphilis.)

The location of the point of maximum intensity of the diastolic murmur has also been used as a means of differential diagnosis because in syphilitic aortic insufficiency, the murmur is heard best at the second right intercostal space, whereas in rheumatic aortic insufficiency, the diastolic murmur is heard best at the third left intercostal space However, this is not an absolute point of differentiation, and is probably due to the fact that in rheumatic heart disease there is more clockwise rotation than in syphilitic heart disease, so that the aorta is rotated more to the left in rheumatic heart disease

Course and Prognosis.—Patients with syphilitic aortic insufficiency may be symptomless for many years However, with the development of heart failure, the course may become rapidly downhill. However, many patients with syphilitic aortic insufficiency and heart failure live many years with proper treatment of the heart failure. An early sign of left-sided heart failure in a patient with cardiovascular syphilis is the development of attacks of paroxysmal nocturnal dyspnea (page 236)

Subacute bacterial endocarditis may also become engrafted on a syphilitic aortic valve. However, in such cases, there is usually associated rheumatic involvement of the valve

Treatment.—See page 552.

SYPHILITIC AORTITIS COMPLICATED BY CORONARY OSTIAL STENOSIS

Coronary ostial stenosis usually occurs in association with aortic insufficiency, and it is difficult if not impossible to ascribe symptoms or signs to the ostial stenosis itself. However, ostial stenosis may occur without aortic insufficiency if the coronary arteries arise from an abnormal position in the aortic wall above the sinuses of Valsalva.

Symptoms.—Coronary ostial stenosis may produce no symptoms. However, angina pectoris may occur due to the inadequate coronary blood flow through the narrowed or occluded vessels.

Signs.—The *physical signs which are present are due to the associated* aortic insufficiency. When attacks of angina pectoris occur, the electrocardiogram may show the typical patterns of myocardial anoxia (page 297).

Diagnosis—The occurrence of anginal symptoms in patients with syphilitic aortic insufficiency is suggestive of coronary ostial stenosis. However, if hypertension is present and if the patient is over fifty years of age, it is very possible that coincidental coronary atherosclerosis and not syphilis is the cause of the angina pectoris, even though the aortic insufficiency is syphilitic in origin.

Course and Prognosis.—The occurrence of coronary ostial stenosis is a poor sign and death usually occurs in a few years. Sudden death is also not uncommon, due to acute myocardial anoxemia. However, myocardial infarction is rare, and when it does occur, it may be due to coincidental coronary artery disease rather than to syphilis

Treatment.—See page 552.

SYPHILITIC ANEURISMS OF THE AORTA

Syphilitic aneurisms of the aorta may occur in as much as 30 per cent of cases of cardiovascular syphilis. The aneurism may be fusiform but it is usually saccular, either single or multiple Its diameter may vary from a few centimeters to more than 20 centimeters Occasionally, smaller "daughter" aneurisms project from the main aneurismal mass. The saccular aneurisms are often filled more or less with a laminated blood clot which may undergo calcification Occasionally, part of the thrombus may break off, causing systemic embolization. The heart itself is not affected by an aneurism of the aorta, and when cardiac enlargement is present in association with an aneurism, the enlargement is due to some other condition The most common sites of the syphilitic aneurisms are the ascending aorta and the aortic arch. Less frequent sites are the descending and abdominal aorta respectively. The aneurism usually involves the convex portion of the aortic arch Syphilitic aneurisms of the sinuses of Valsalva, of the innominate and other large arteries may also occur.

The symptoms and signs of aneurism depend on the location and size of the aneurism. Small aneurisms involving the intrapericardial portion of the ascending aorta, including the sinuses of Valsalva, may rupture without any previous symptoms. On the other hand, symptoms may be marked and physical signs minimal in an aneurism of the arch of the aorta which is *deeply seated and in close relation to the trachea*, esophagus, left bronchus, and systemic and sympathetic nerves For purposes of description the aneurisms in various locations shall be described separately.

SYPHILITIC ANEURISMS OF THE SINUSES OF VALSALVA

One or all of the sinuses may be involved with syphilitic aneurisms. The clinical picture produced by these aneurisms is described on page 429.

SYPHILITIC ANEURISMS OF THE ASCENDING AORTA

Symptoms.—Symptoms may be minimal even though the aneurism may be quite large, and obvious on physical examination. This is the reason the older clinicians called these aneurisms, "aneurisms of physical signs" However, a sense of dull substernal pain or pressure may be present, especially if the sternum and ribs are being eroded by the aneurism

Signs.—An abnormal pulsation may be present over the base of the heart, especially over the manubrium, or to the right or left of the sternum in the second intercostal space. The pulsation, systolic in time, is heaving and has an expansile quality. In association with this, percussion reveals abnormal dullness or flatness, either over the manubrium which is ordinarily resonant, or to the right or left of the sternum. This is especially significant if the abnormal pulsation and dullness are noted to the right of the sternum, because a dilated pulmonary artery due to a rapidly beating heart in a thin person, or in hyperthyroidism, anemia, or in congenital lesions, such as patent ductus, Eisenmenger complex, idiopathic dilatation of the pulmonary artery, interauricular septal defect, *etc*, may cause a systolic pulsation, murmur and even a thrill, and dullness on percussion, to the left of the sternum at the base of the heart (see also pages 36 and 156) The aneurism, if large, may displace the heart to the left. Pulsation of the aneurism may be minimal if it is filled with a thrombus.

In cases where the aneurism has eroded the sternum and the ribs, it may lie directly beneath the skin and protrude as a large, round mass, and the overlying skin may crack and ooze blood Fortunately such aneurisms have become rare, due to early recognition and treatment of syphilis

A systolic thrill and murmur over the aneurism may or may not be present, along with a characteristic diastolic shock, which consists of a short, sharp impulse coincident with diastole A diastolic thrill or murmur, if present, is due to coincidental aortic valvular disease.

Fluoroscopic and X-Ray Examination.—An aneurism can be recognized on fluoroscopic or *x*-ray examination as a dense mass with a smooth outline, contiguous with the aorta when viewed in all positions. Expansile systolic pulsations are usually present, but may be absent if a large thrombus has formed within the aneurism

Diagnosis.—Occasionally it is extremely difficult to differentiate an aneurism from a mediastinal tumor which lies adjacent to the aorta, because the tumor may show transmitted pulsations from the aorta. In such cases, angiocardiography may be necessary. An aneurism of the ascending aorta due to arteriosclerosis of the aorta rather than to syphilis may occur, but arteriosclerotic aneurisms are very rare in the ascending aorta, and become more common in the distal portions of the aorta, especially the abdominal aorta A dilated ascending aorta due to dynamic dilatation of the aorta (page 536) should not be mistaken for a fusiform aneurism.

Course and Prognosis.—Regardless of the site of the aneurism, a patient with an aneurism may die in one of three ways: from some independent condition; from rupture of the aneurism, or from mechanical compression of viscera, produced by the aneurism About one-half the deaths are caused by rupture of the aneurism

An aneurism of the ascending aorta may compress the superior vena cava producing congestion of the face and upper extremities with cyanosis and even edema (superior vena caval syndrome, page 672). It may compress the right bronchus and lung, giving rise to pulmonary symptoms of cough, hemoptysis and fever, due to atelectasis, pneumonitis, even bronchiectasis or a lung abscess (so-called aneurismal phthisis). Even the pulmonary artery may be compressed by an aneurism of the aorta, resulting in the clinical picture of cor pulmonale.

The aneurism often ruptures into the pericardium which completely encloses the ascending aorta. However, the aneurism may rupture externally, or into the right bronchus, also causing sudden death. Rupture into the lung tissue, however, may result in repeated bouts of hemoptysis rather than sudden death. Rupture into the pulmonary artery or into the superior vena cava or right auricle may produce characteristic syndromes:

Rupture of an Aortic Aneurism into the Pulmonary Artery.—The onset is sudden with extreme dyspnea and a sense of smothering tightness and fullness in the chest. The patient may go into shock and die almost instantly, but some patients recover and may live several months or more. The dyspnea is severe and continuous and is out of proportion to the minimal rales which may be present in the chest. The cause of this intense dyspnea is probably the sudden pulmonary congestion which stimulates the Hering-Breuer reflex

Examination reveals a purring systolic and diastolic thrill over the base of the heart, most intense during systole A long, harsh continuous murmur, with the point of maximum intensity at the third intercostal space, 1 to 3 cm. to the left of the sternal border is also present. The systolic phase of the murmur is peculiarly harsh and long, whereas the diastolic phase is short in duration, and is transmitted downward for only a few centimeters along the left sternal border. The murmur is best heard with the patient sitting and leaning slightly forward. Capillary pulsation, a collapsing pulse, Duroziez's sign and other manifestations of a wide pulse pressure appear. Cyanosis is absent or minimal.

A similar clinical picture occurs when an aortic aneurism ruptures into the right auricle or right ventricle. In such cases, the thrill and murmur are found best near the midsternum and are transmitted downward to the liver and umbilicus

Rupture of an Aortic Aneurism into the Superior Vena Cava.— A continuous thrill and murmur occur just as when an aortic aneurism ruptures into the pulmonary artery or right heart, but here, the continuous murmur is heard best to the right of the sternum in the first and second intercostal spaces In addition, the face becomes swollen, blue and suffused, and the patient may look as if he were being strangled. Venous distention, edema and cyanosis of the upper half of the body also appear, but the lower body remains normal. However, if acute right-sided heart failure occurs, the liver may become markedly distended, with systolic pulsation, and edema of the lower extremities may appear

When an aortic aneurism ruptures into the inferior vena cava, it is the lower half of the body which shows the cyanosis and edema.

SYPHILITIC ANEURISMS OF THE ARCH OF THE AORTA

Aneurisms of the arch of the aorta have been called aneurisms of symptoms because the arch of the aorta lies in front of the trachea and esophagus and sympathetic plexi, above the left bronchus, has the left recurrent laryngeal nerve curving around it, and the left phrenic nerve in contact with its anterior surface, so that even a small aneurism here can cause pressure symptoms early. On the other hand, the aortic arch is so deeply placed that physical signs may be minimal.

Symptoms.—A dry, harsh, grating cough may develop when the trachea *or left bronchus is compressed. In addition, blood-streaked expectoration* may develop. When the left recurrent laryngeal nerve is compressed and paralysis of the left vocal cord develops, dysphonia, hoarseness, or a ringing, brassy or croupy cough may appear. The right vocal cord can also become paralyzed. Pressure on the left bronchus may result in bronchial stenosis with atelectasis and signs of pulmonary inflammation. Pressure on the esophagus may cause a persistent dysphagia. However, transient dysphagia may develop in the early stages of the aneurism due to esophageal spasm resulting from irritation of the recurrent laryngeal nerve which supplies the esophagus as well as the larynx. Irritation of the phrenic nerve may result in hiccup or even paralysis of the left leaf of the diaphragm.

Signs.—An abnormal pulsation may sometimes be felt by pressing in the suprasternal notch or over the manubrium. However, a forceful or dilated aorta can also give these signs. Abnormal dullness over the manubrium may also be present, if the aneurism is large.

Inequality of the pupils may occur as a result of pressure on the sympathetic nerves. *The pupil on the affected side may be dilated or contracted,* depending on whether the sympathetic fibers are being irritated or have been destroyed by the aneurismal pressure. However, changes in pupillary size may be a direct result of the syphilis. In such cases, the light reflex and power of accommodation are also lost, whereas if the inequality is due to an aneurism, the light reflex is present. Irritation of the sympathetics may also cause abnormal sweating in the upper extremity or even on one side of the face.

Bilateral inequality of the pulse and blood pressure may result. The right radial pulse will be smaller than the left, if the innominate artery is compressed. Similarly, if the left subclavian artery is compressed, the left *pulse will be smaller than the right. In* this connection it is preferable to palpate the brachial arteries rather than the radials, whose position and force of pulsation are more subject to variation. However, inequality of the pulses does not necessarily indicate an aneurism, even if syphilis is present. The reason for this is that the mesaortitis may extend to the innominate or left subclavian artery and produce constriction or even occlusion of the vessel. Inequalities in the pulse may also occur in other ways (page 140).

The aneurism can also cause a delay in the time of appearance of the pulse wave. Thus, a delay in the time of appearance of the left pulse will occur if the aneurism lies between the origin of the innominate and left subclavian arteries. The delayed pulse also gives the sensation of subsiding

more slowly than that on the unaffected side Bilateral variations of blood *pressure of more than 10 mm. may also appear.* Even this is not pathognomonic of aneurism, and may occur with pressure of a tumor on the subclavian or axillary artery, with the scalenus anticus syndrome, (page 140) *etc.* If the aneurism becomes adherent to the trachea, a tracheal tug (Oliver's sign) (page 147) may be elicited

Fluoroscopic and X-Ray Examination.—A round mass is seen contiguous with the arch of the aorta It may or may not pulsate. Erosion of the anterolateral aspect of the fourth, fifth and sixth thoracic vertebræ may be present. The trachea and esophagus may be displaced

Diagnosis.—A thymic or other *anterior mediastinal mass may simulate* an aneurism of the aortic arch, and require angiocardiography for differential diagnosis An aneurism of the innominate artery (see below) may also simulate an aneurism of the arch of the aorta. As a matter of fact, aneurisms of both vessels may be present simultaneously.

Course and Prognosis—An aneurism of the arch of the aorta may *rupture* into the left bronchus, the trachea, the esophagus, causing sudden death, or into the pulmonary artery or superior vena cava, producing an *a-v* fistula Rupture often occurs before the aneurism becomes very large However, an aneurism of the arch may be found as an incidental finding at autopsy

Treatment—See page 552.

SYPHILITIC ANEURISMS OF THE INNOMINATE ARTERY

Symptoms.—The aneurism may press on the right brachial plexus, causing severe pain radiating along the right upper extremity. Pressure on the right cervical sympathetics may produce myosis and a right lid lag (Horner's syndrome)

Signs—A pulsating mass can often be found behind or just above and to the right of the right sterno-clavicular joint, which may be eroded and displaced forward by the aneurism The aorta may be displaced downward The trachea may be displaced to the left, and pressure on the superior vena cava may produce congestion, cyanosis or edema of the head and upper *extremities A thrill and murmur may be elicited* over the aneurism. The aneurism causes a delay in the spread of the pulse wave to the radial artery, and the right radial pulse is delayed.

Diagnosis.—An aneurism of the innominate artery can be simulated by a dilated and tortuous right common carotid artery which can pulsate *markedly in the right supraclavicular fossa (page 148) However,* the right radial pulse is not delayed in this condition. (The innominate artery can also become buckled in hypertension)

Course and Prognosis—Rupture into the surrounding hollow or vascular structures may occur.

Treatment.—See page 552.

SYPHILITIC ANEURISMS OF THE DESCENDING THORACIC AORTA

***Symptoms.**—If the aneurism lies just below the arch it may cause pres*sure on the left bronchus or esophagus. However, aneurisms of the de-

scending aorta usually expand backwards, pressing on the spine and intercostal nerves Pain is often the chief manifestation of the aneurism It may be dull and aching and localized, due to erosion of bone, or it may be sharp and shooting, radiating around the chest, due to nerve irritation

Signs.—There may be practically no abnormal physical signs even though a large aneurism of the descending aorta is present. However, abnormal dullness on percussion, and a systolic pulsation may be found in the left interscapular space, or below the angle of the left scapula The aneurism may also erode the posterior ribs and produce a pulsating mass in the back Rarely, the aneurism projects forward and causes an abnormal epigastric pulsation.

Diagnosis—Diagnosis is easily made by x-ray examination. If the aneurism projects backwards it can be best visualized in the L A O position If it projects forward, it can be best seen in the R A O position. Erosion of the anterior surfaces of the vertebræ is a confirmatory sign of the aneurism Differentiation from an arteriosclerotic aneurism of the descending aorta may be impossible clinically

Course and Prognosis—An aneurism of the descending aorta may be present for ten or more years without causing any serious disturbances It may rupture externally, into the right or left pleural cavity, into the esophagus, the inferior vena cava (see page 548) or into other adjacent structures

Treatment.—See page 552

SYPHILITIC ANEURISMS OF THE ABDOMINAL AORTA

Symptoms—An aneurism of the abdominal aorta may cause pressure on the spine and produce dull, boring back pain, paresthesias and even a paraplegia Pressure on the hollow abdominal organs may produce abdominal pain or colic or symptoms of intestinal obstruction However, the aneurism may often be symptomless.

Signs—On abdominal palpation, an expansile mass may be felt. A systolic thrill and bruit are also usually present over the mass X-ray examination, especially in the lateral position, visualizes the aneurism well. In addition, confirmatory erosion of the vertebræ may be present.

Diagnosis—The chief difficulty in diagnosis is to differentiate a syphilitic aneurism of the abdominal aorta from an arteriosclerotic aneurism, which is more common Arteriosclerotic aneurisms of the abdominal aorta usually occur in patients over fifty or sixty years, whereas syphilitic aneurisms are almost always seen in younger people In addition, a syphilitic aneurism of the abdominal aorta is often associated with an aneurism of the thoracic aorta.

The forceful abdominal pulsations of a normal aorta in a thin person should not be confused with an abdominal aneurism However, in such cases, a local expansile mass is not present.

Course and Prognosis—An aneurism of the abdominal aorta may be present for many years without causing serious disturbances. However, retroperitoneal oozing may occur with the formation of a retroperitoneal hematoma which may reach massive dimensions and may cause ecchymoses of the skin over the inguinal, iliac and scrotal regions, and obliteration of the

psoas muscle shadow on *x*-ray examination. In addition, fatal rupture either into the peritoneal cavity or into one of the hollow organs may occur. The aneurism does not rupture externally.

THE TREATMENT OF CARDIOVASCULAR SYPHILIS

The treatment of cardiovascular syphilis can be considered under three headings: (A) active treatment to arrest the low-grade syphilitic process which is probably present in the aorta and related structures, and to prevent further progression of the lesions; (B) treatment of heart failure, if present, regardless of whether the failure is due to the syphilitic heart disease or associated heart disease; and (C) the treatment of syphilitic aneurisms. Cure in the usual sense cannot be obtained because organic damage which is already present does not disappear even though all treponemata are destroyed.

Penicillin is the drug of choice. Aqueous procaine penicillin can be given intramuscularly daily or every two days in a dose of 600,000 units for twenty injections. This is a total dose of 12,000,000 units.

Another schedule that can be used is to give 900,000 units of aqueous procaine penicillin intramuscularly every two or three days for twelve injections, a total dose of 10,800,000 units.

Larger doses of penicillin are not needed. One cannot use the blood serology as a guide to treatment, because a positive reaction may persist even though the therapy is successful.

Two complications may arise from the penicillin therapy, namely, the *Jarisch-Herxheimer reaction*, and the so-called *therapeutic paradox.*

The Jarisch-Herxheimer Reaction.—This reaction occurs after the first injection of a potent antisyphilitic substance, such as the arsphenamines, but has been reported after bismuth and penicillin. It consists of a flare-up of the syphilitic lesions, together with malaise and fever, twelve to twenty-four hours after the injection. Thus, if a syphilitic plaque is located at the mouth of a coronary artery, swelling of the plaque due to the Jarisch-Herxheimer reaction may cause complete occlusion of the vessel and may precipitate an intense attack of angina pectoris.

The reaction may be avoided by starting treatment with small doses of penicillin, or better still by beginning treatment for a month or two with bismuth, because it is not yet known what constitutes a small dose of penicillin when it is used as an antisyphilitic drug.

When penicillin was first used in the treatment of cardiovascular syphilis, it was suggested that the Jarisch-Herxheimer reaction could be avoided by giving an intramuscular injection of 2 cc. bismuth subsalicylate in oil for three or more weeks before beginning penicillin. Most syphilologists now believe that this is not necessary. However, occasionally a patient will develop the Jarisch-Herxheimer reaction when penicillin is used without prior bismuth therapy.

The Therapeutic Paradox.—In the therapeutic paradox, rapid healing of the syphilitic lesion occurs with such accelerated scar tissue formation that coronary ostial stenosis or aortic insufficiency may be aggravated, thus leaving the patient with arrested syphilis but with a worsened cardiovascular system.

B. The Treatment of Associated Heart Failure.—If heart failure is present, it should be treated according to the conventional methods.

C. Treatment of Syphilitic Aneurisms.—Treatment of saccular aneurisms is generally unsatisfactory, and no specific treatment can be used for fusiform dilatation of the aorta. Wiring of a saccular aneurism by inserting a coil of gold or silver or even platinum wire into the aneurism and passing a small galvanic current through the wire to produce thrombosis of the aneurismal sac has been used successfully in some cases. Another form of treatment that has been used is to surround the sac with cellophane, or even fascia lata, in the hope of producing a dense fibrous scar around the sac.

SYPHILITIC MYOCARDITIS

The only specific form of myocarditis in syphilis is the development of a gumma which may be small or large, localized and single, or multiple and diffusely scattered through the myocardium. Gummata may be found anywhere in the heart but occur most frequently in the wall of the left ventricle near the base, and in the interventricular septum. A gumma of the interventricular septum may injure the bundle of His and may produce incomplete or complete *a–v* block. Rarely, a myocardial aneurism or rupture of the ventricle or of a papillary muscle occurs from a gumma. The gumma may also extend to the valvular orifices, especially to the aortic valve.

Gummata produce no characteristic symptoms or signs.

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Chapter 36

HYPERTENSIVE HEART DISEASE

Hypertension can be defined as the elevation of the systolic and/or diastolic blood pressure above the arbitrary level of 150/90, or even 140/90 in young people. It is the most common cause of cardiac enlargement and heart failure

Classification.—Hypertension may occur in many diverse conditions, and many classifications have been proposed, none of which is completely satisfactory For present purposes, the more common causes of hypertension can be classified in the following way:

1 Hypertension of Unknown Etiology (primary hypertension, hyperpiesia)
   A. Essential Hypertension, page 557.
   B Malignant Hypertension, page 561.
2. Hypertension Associated with Kidney or Genito-Urinary Disease, page 577.
   A. Acute and Chronic Glomerular Nephritis, page 735
   B Polycystic Kidneys.
   C Diabetic Glomerulonephrosis.
   D Renal Arterial or Venous Occlusion (thrombosis or embolism) or Aberrant Renal Artery.
   E Hydronephrosis, Pyelonephritis, Prostatic Obstruction
   F Toxemias of Pregnancy, page 756.
   G. Diffuse Vascular Disease (lupus erythematosus, periarteritis nodosa, *etc*) with Renal Involvement.
3 Hypertension Associated with Endocrine Disturbances
   A Adrenal Medullary Tumors (Pheochromocytoma, and Paraganglioma) page 701.
   B. Cushing's Syndrome, page 694.
4 Hypertension Associated with Intracranial Disease
   A Brain Tumors
   B. Infections of the Brain Stem Poliomyelitis, etc.
   C Cerebral Trauma, *etc*
5 Hypertension Due to Miscellaneous Conditions.
   A. Coarctation of the Aorta, page 453
   B. Chronic Aortic Valvular Disease, *etc*

Etiology.—On page 29, are described the factors which determine the blood pressure, the most important of which is the peripheral resistance, which is increased in almost every type of clinical or experimental hypertension. The increased peripheral resistance is produced by arteriolar constriction, but the cause of this is unknown for the most part. In some conditions, such as pheochromocytoma, there is an increased amount of circula-

ting epinephrine which produces the arteriolar constriction. In cases of brain tumors, the increased intracranial pressure stimulates the vasomotor center. In Cushing's disease, adrenal cortical tumors, arrhenoblastoma, *etc.*, there is an excess of adrenal cortical steroids in the blood. However, in essential and malignant hypertension and the hypertension due to most of the other conditions mentioned above, the mechanism by which arteriolar constriction occurs is unknown, although the following theories have been proposed:

1 **The Rôle of the Kidney in Relation to Essential Hypertension** —Goldblatt was the first to produce chronic hypertension in the dog, similar to essential hypertension in man, by partially clamping the renal artery. It was later shown that chronic hypertension in the dog could also be obtained by wrapping the kidney in cellophane or silk, producing a constricting perinephritis The relation of such kidney disturbances to the development of hypertension has been explained as follows: If vasoconstriction and especially if renal arteriolar constriction occurs, the kidney blood flow decreases and an enzyme, renin, is released Renin is not a vasoconstrictor but it causes the conversion of alpha-2-globulin (hypertensinogen, or renin substrate) into hypertensin (angiotonin), which is an active vasoconstrictor, and which thus produces an increased blood pressure Hypertensin can be destroyed by the enzyme, hypertensinase (angiotoninase) in the blood and other tissues The final result of long-continued vasoconstriction is renal arteriosclerosis, which produces a further decrease in kidney blood flow, and thus aggravates the hypertension

A weakness of this theory is that the renal blood flow in the human is usually normal in early cases of essential hypertension. Further, it has not been possible to demonstrate increased quantities of renin or hypertensin in the blood in cases of essential hypertension. Goldblatt believed that the primary disturbance in the kidney was the development of arteriolosclerosis which resulted in renal disfunction and renin production However, renal biopsy studies in cases of early essential hypertension have failed to reveal any significant pathological changes. To complicate further the relation between the kidneys and hypertension, it has recently been demonstrated that when both kidneys are removed in dogs (renal function being maintained by an electrolyte-free diet and the use of an artificial mechanical kidney) hypertension, instead of hypotension develops

There is some evidence that norepinephrine, from the adrenal medulla (page 701), may be a cause of essential hypertension. Norepinephrine is a general vasoconstrictor. It is inactivated by the enzyme, amine oxidase, which is present in most tissues of the body. Essential hypertension therefore may be due to a deficiency of this enzyme.

Another theory that involves the kidney is that hypertension may develop from an imbalance between a hepatic vasodepressor material, VDM, and a kidney vasoexcitor or vasoconstrictor material, VEM. Both these substances are absent in the blood of normal people, but appear in cases of essential and malignant hypertension, and in hypertension experimentally produced by decreasing the renal blood flow.

2. **Endocrine and Electrolyte Factors in Relation to Essential Hypertension.**—Hypertension and nephrosclerosis can be produced experimentally

in animals by administering adrenal steroid hormones, such as desoxycorticosterone, or pituitary adrenocorticotrophic hormone (ACTH), especially if the animal is placed on a high-salt, high-protein diet. This can be prevented by a low-salt or low-protein diet. In man, it has also been shown that the administration of desoxycorticosterone and salt to patients with Addison's disease often results in hypertension, and when it is given to hypertensive patients, a further increase in blood pressure occurs The increased adrenal cortical activity in Cushing's syndrome has already been mentioned

3 **Psychogenic and Neurogenic Factors in Relation to Essential Hypertension** —*It is known that disturbing psychogenic stimuli can produce generalized* vasoconstriction, and some psychiatrists have suggested that hypertension may be initiated by emotional stress, but that if it continues it produces sufficient renal arteriolar constriction and renal arteriosclerosis to result eventually in hypertension of renal origin.

In this connection, there has been described a characteristic personality trait of hypertensive patients, namely, that hypertensive patients show external friendliness and self-control, beneath which there exists intense latent hostility and aggressiveness which is only partially repressed Coupled with this is a feeling of anxiety This occurs because the patient is afraid that if he were to give vent to his aggressive impulses he would jeopardize his position or security in his family, or in his business or social circles.

4 **Other Factors in Relation to Essential Hypertension.**—Hypertension is often familial, and may have an hereditary factor. Similarly, many hypertensive patients are obese and stocky

Summary.—Although the cause of essential hypertension is still not known, the following factors seem to be of importance: Repressed psychic disturbances can lead to increased activity of the sympathetic nervous system Long-continued sympathetic stimulation can produce renal ischemia and can stimulate the adrenal cortex Renal ischemia leads to *the production of pressor substances and in this way produces hypertension* The hypertension itself causes arteriolar sclerosis, especially in the kidneys This results in more renal ischemia Adrenal cortical activity itself can cause hypertension Variations in the type and characteristics of the hypertension are due to the degree of renal or adrenal involvement, the degree of primary kidney disease and the extensiveness of arteriosclerosis throughout the body and to other factors not yet known

Pathological Physiology.—The primary effect of the increased peripheral resistance is to increase the work of the left ventricle, which dilates and hypertrophies. The degree of hypertrophy is variable. The weight of the heart is often more than 500 grams (normal 200 to 350 grams), and may even exceed 700 or 800 grams When dilatation of the left ventricle occurs, the mitral valve ring may become stretched, producing functional mitral insufficiency and an increase in pressure and dilatation of the left auricle. This becomes aggravated when left-sided heart failure develops, and the increased left auricular pressure is transmitted to the pulmonary circulation and eventually to the right side of the heart, so that in the late stages of hypertensive cardiovascular disease, right ventricular dilatation and hypertrophy may also be present. Dilatation, elongation and tortuosity of the aorta also occurs.

The Relation Between Arteriosclerosis and Hypertension.—In association with the hypertension, some degree of arteriosclerosis occurs in the arteries and arterioles throughout the body. This is discussed in the following chapter

Symptoms.—Hypertension is frequently symptomless. However, occipital or vertex headaches, dizziness and tinnitus are common The headache is apparently due to stimulation of pain-sensitive nerve endings in dilated cerebral arteries Epistaxis may also occur if the blood pressure rises suddenly Vague precordial pain, palpitation, restlessness, or a feeling of nervous tension are also frequent. These symptoms of hypertension are very similar to those of neurocirculatory asthenia because the hypertensive patient is a hyper-reactor and responds to minor stimuli with excess emotional reactions in addition to an excess elevation of blood pressure (This tendency to hyper-react has been used as the basis of the cold-pressor and other tests to determine persons with potential hypertension, page 32)

Sudden marked elevation of blood pressure in a patient with essential hypertension, malignant hypertension, and even glomerular nephritis may produce the clinical picture of hypertensive encephalopathy, which consists of severe headache, vomiting, epileptiform seizures, and coma. Papilledema due to the increased intracranial pressure, also appears. Vision may be temporarily lost for several hours or days Hypertensive encephalopathy can be produced by either spasm of the cerebral arteries or by cerebral edema

Signs.—**The Blood Pressure** —The systolic pressure may be slightly over 150 mm or more than 200 or even 300 mm The diastolic pressure may be as low as 90 mm or less It is usually 100 mm , and in some cases may rise to 160 mm or more, especially when the systolic pressure approaches or exceeds 250 mm The blood pressure may fluctuate widely, even in cases where the level has been over 200 mm for a long time. Patients with minimal hypertension or latent hypertension show a marked rise with the cold pressor or other tests (page 32). The fall of pressure with sodium amytal, or spinal anesthesia or adrenolytic drugs, such as tetraethylammonium chloride, dibenamine, *etc* , has been used by some to determine whether a patient will respond effectively to sympathectomy (page 576)

It has been stated that a diastolic pressure of more than 130 mm. is a bad prognostic sign. However, I have observed very high diastolic pressures, associated with high systolic pressures in elderly patients who lived for many years In a young person, a continued rise in diastolic pressure to 130 mm. or more usually indicates the onset of malignant hypertension (page 561).

Ophthalmoscopic Examination —The eye grounds may be normal or may show arteriosclerotic changes, or arteriosclerotic or hypertensive retinopathy (page 146) Wagener and Keith have graded essential and malignant hypertension by means of retinal changes in the following way

Grade 1.—Retinal changes consist of mild narrowing (spasm) or mild arteriosclerotic changes

Grade 2.—The changes are more marked than in grade 1, but hypertensive retinopathy (hemorrhages and exudates) is not present. There is moderate to marked arteriosclerosis with increased light reflex, *a–v* compression and localized irregular narrowing of the arterioles

Grade 3.—Cotton-wool patches and hemorrhages are superimposed on the sclerotic or spastic vessels.

Grade 4—Edema of the disc is present in addition to the above abnormalities. (This is a sign of malignant hypertension.)

Physical Findings.—Physical examination may reveal minimal abnormalities or the physical signs of left ventricular hypertrophy, and of peripheral arteriosclerosis. The radial pulse is forceful and full. The radial artery, the brachial artery, and other peripheral arteries may be tortuous, thickened and stiff and reveal beading on palpation. The markedly dilated right common carotid artery may be so prominent in the right supraclavicular fossa as to resemble an aneurism.

In the heart, the forceful apical impulse becomes displaced beyond the left midclavicular line, and downward, and occupies a wider area than normal. An accentuated aortic second sound is common. An apical systolic murmur frequently appears, due to dilatation of the mitral valve ring and functional mitral insufficiency. An aortic systolic murmur may also appear, either due to dilatation of the aortic valve ring or to the rapid flow of blood through a dilated aorta. An aortic diastolic murmur may even appear due to dynamic dilatation of the aorta (page 536).

Occasionally, the second sound at the base is heard better to the left of the sternum than to the right. This has been described as a sign of left-sided heart failure in a hypertensive patient, but it may merely indicate that the aortic second sound is being transmitted to the left rather than to the right. This can occur with clockwise rotation of the heart.

Fluoroscopic and X-Ray Examination.—Some degree of enlargement of the left ventricle, with prominence of the aortic knob and some degree of tortuosity, elongation or dilatation of the aorta may be present (pages 181, and 191). With the onset of heart failure, generalized cardiac enlargement occurs.

Electrocardiogram.—In the early stages of hypertension, the tracing may be completely normal. Later, *RS–T* and *T* signs of left ventricular strain, or high voltage of the *QRS*, due to left ventricular hypertrophy, or both may appear. The electrocardiographic patterns of strain may disappear spontaneously or after medical therapy or sympathectomy, but if the *RS–T* and *T* deviations are marked and are associated with large, wide *QRS* complexes, the pattern usually remains fixed. There is no constant relation between the electrocardiographic patterns and the height of the blood pressure.

Laboratory Tests.—The urine may contain some albumin and a few granular and hyaline casts, but no red blood cells. The specific gravity remains high, or if low, the patient is able to concentrate, and the urine concentration test is normal. There is no nitrogen retention in the blood. However, in the late stages of hypertension, if nephrosclerosis has developed, nitrogen retention and uremia may occur.

Diagnosis.—Although most patients with an elevated blood pressure have essential hypertension, the other causes of hypertension should not be overlooked. In a brain tumor, hypertension and headache and other symptoms and signs of increased intracranial pressure are associated with papilledema without sclerotic changes in the retina or signs of hemorrhage

or cotton-wool exudates. (Rarely, isolated papilledema occurs in essential hypertension) Cushing's syndrome is described on page 694 In other cases, examination of the abdomen may reveal an adrenal or ovarian tumor which may be the cause of the hypertension, or signs of a large infected kidney on one side.

When hypertension is present, the blood pressure of the lower extremities should be routinely taken, or the femoral arteries palpated, to rule out coarctation of the aorta.

Examination of the urine and blood is helpful in diagnosing hypertension due to chronic glomerular nephritis, which often shows marked anemia, often some nitrogen retention in the blood and urinary findings of a low fixed specific gravity, albumin, hyaline and granular casts, and some red blood cells However, similar findings occur in malignant hypertension and the differential diagnosis of malignant hypertension from chronic glomerular nephritis may be quite difficult. However, in malignant hypertension, the blood pressure is usually higher, the left ventricle larger, the aorta more tortuous and longer, and the electrocardiogram more often shows signs of left ventricular hypertrophy and strain than in chronic glomerular nephritis Furthermore, signs of advanced heart disease are usual in malignant hypertension, and indistinct or absent in nephritis

The cardiac murmurs of hypertensive cardiovascular disease should not be misinterpreted as signs of organic valvular disease. Finally, paroxysmal attacks of palpitation, flushing or sweating associated with a marked rise in blood pressure are suggestive of a pheochromocytoma (page 701). However, pheochromocytoma may occur with a chronically sustained high blood pressure

Course and Prognosis.—Hypertensive heart disease is slowly progressive, and the patient may live ten, twenty, or more years without developing serious complications Death is caused by heart failure in about 50 per cent of the cases, by cerebrovascular accidents in about 20 per cent of the cases, by coronary artery occlusion and myocardial infarction in about 20 per cent, and by nephrosclerosis, uremia and miscellaneous conditions in the remaining 10 per cent.

Malignant Hypertension —In a small percentage of young persons, rapidly progressive changes may appear, producing the clinical picture known as malignant hypertension Symptoms include severe occipital headaches or hypertensive encephalopathy, rapid loss of weight, impairment of vision, and nycturia.

There is a rapid rise in blood pressure, the diastolic pressure usually rising to 140 mm. or more Marked enlargement of the heart is present, due to massive left ventricular hypertrophy. Examination of the eye grounds reveals hypertensive neuroretinopathy with hemorrhages, exudates and papilledema The urine shows albumin, granular and hyaline casts, many red blood cells, even a macroscopic hematuria, and a specific gravity which rapidly becomes low and fixed, the patient being unable to concentrate the urine A severe hypochromic anemia may develop.

When malignant hypertension develops, death usually occurs from uremia, occasionally from heart failure, often in a few months, or within four years. The average age at death is about forty years At autopsy, marked

Grade 3.—Cotton-wool patches and hemorrhages are superimposed on the sclerotic or spastic vessels.

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Diagnosis.—Although most patients with an elevated blood pressure have essential hypertension, the other causes of hypertension should not be overlooked. In a brain tumor, hypertension and headache and other symptoms and signs of increased intracranial pressure are associated with papilledema without sclerotic changes in the retina or signs of hemorrhage

During the first period of "regulation" on the diet, the patient should be under constant medical supervision and blood and urine chemistry should be checked frequently because renal failure or uremia may develop Rest in bed is neither necessary nor desirable, unless severe heart failure is present.

It is not unusual for the weight to decrease more or less markedly during the first twenty days. The reason for this weight loss may be that the amount of food given does not cover the caloric requirements; in this case the amount of rice, fruit and sugar must be increased, unless reduction of weight is indicated. Another reason may be that the patient does not eat the full amount of his diet during the first period of adjustment Another cause of weight loss is the loss of visible or invisible edema.

As a rule, the diet should be continued without modification until those conditions which were the indication for its use have disappeared (see also below) Then small amounts of nonleguminous vegetables, potatoes, lean meat or fish (all prepared without salt or fat) may be added In cases where a critical condition of the cardiovascular system or kidneys is present, it has been suggested that the strict rice diet be continued indefinitely However, this may be dangerous because the diet usually causes a negative protein balance of the body, so that protein other than that contained in rice must be added if the diet is to be continued over a period of months or years (Also see page 564)

The following menu is an example of a day's diet

Breakfast

1 cup of orange juice
2 cups of boiled rice
22 grapes

Lunch

3 cups of rice with 2 tablespoons of honey
1 cup of orange juice
2 peaches (fresh or canned)

Supper

2 cups of rice
2 cooked apricots
1 cup of prune juice
½ a cantaloupe (or other fruit in season)

Night

1 cup of orange juice
3 plums or prunes

Modified Rice Diet.—For patients who rebel at the strict rice diet, the following foods, which have a low-sodium and low-protein content can be given in addition to the rice, fruit and fruit juices: cereals, such as oatmeal, cream of wheat, farina, instant ralston, *etc* ; all vegetables, except beets, kale, celery, and spinach, low-sodium bread or matzohs; coffee and tea in small quantity.

Patients on the rice diet or its modifications must be warned of sudden weakness or other untoward symptoms, because the low-sodium content of the food causes a decreased renal blood flow and may precipitate severe and sometimes fatal uremia In addition, some patients with hypertension and chronic nephritis excrete excess quantities of salt in their urine and may develop an Addisonian-like crisis when placed on a low-sodium diet. Another danger of the diet is that the patient may not remain in nitrogen equilibrium on only 20 grams of protein a day.

Some cardiologists have given weekly and even biweekly injections of mercurials in addition to the low-sodium diet to produce a rapid loss of sodium, but I do not advocate this.

The rice diet or its modification may have to be continued for as long as eight to twelve weeks or longer until improvement occurs. However, if no significant improvement has occurred after twelve weeks, the patient will probably not respond. For patients with moderate hypertension, an ordinary low-sodium diet (page 248) is effective.

Results of the Rice Diet.—Marked decrease in both systolic and diastolic pressures may occur. Papilledema and retinal hemorrhages and exudates may disappear. The heart may shrink in size, and electrocardiographic signs of ventricular strain may disappear. The non-protein nitrogen content of the blood falls, blood cholesterol level often falls greatly if it has been elevated, but may rise (the body can synthesize cholesterol from acetate); plasma protein levels are maintained; blood chloride and sodium values do not change significantly, but the blood potassium level rises slightly.

The rice diet has been used successfully not only in hypertensive heart disease, but in acute and chronic nephritis However, when the kidney function is impaired, the low sodium content of the rice diet may decrease renal blood flow so much that uremia and hyperpotassemia may occur

Diabetes is not a contraindication and it has been stated that patients on the diet may require less insulin. In cases complicated by peptic ulcer, raw fruits may be poorly tolerated, but cooked fruit can be used.

The efficacy of the diet has been subject to much controversy Good results have been claimed by some in as high as 60 per cent of the cases, whereas other investigators believe that the diet has very *little value*, *if* any. In my own experience, the rice diet or its modification, has been of value in about one-third of the patients.

Medical Treatment.—The anti-hypertensive drugs in use can be classified in the following way.

I Drugs Exerting Unknown or Mixed Effects: *thiocyanates*, *sodium* nitroprusside, rauwolfia serpentina, pyrogens, the xanthines, *etc.*

II Drugs Acting Directly on Vascular Smooth Muscle: papaverine, nitrites, *etc*

III Drugs which Interfere with Sympathetic Vasomotor Activity:

A. Adrenergic Blocking Agents: *b-haloalkylamines* (dibenamine, dibenzyline), imidazolines (priscoline, regitine), benzodiozanes (benodaine); ergot alkaloids, *etc*

B Ganglionic Blocking Agents: quaternary ammonium compounds (tetraethylammonium [TEA], methonium compounds, *etc.*)

C. *Centrally-acting Inhibitors of Sympathetic* Vasomotor Activity:

hydrogenated ergot alkaloids, 1-hydrazinophthalazine (hydralazine, apresoline).

D. Agents Inhibiting Afferent Vascular Reflex Paths: the veratrum alkaloids.

Some of these drugs can be considered in more detail.

The xanthines (page 305) have been widely used in hypertensive heart disease, but I believe that they have mostly placebo value. The effect of nitrites (page 304) on blood pressure is only transient.

The thiocyanates (sulfocyanates) have also been widely advocated and just as strongly condemned. They must be given in sufficient doses to obtain a blood level of from 6 to 12 mg. per cent. For this purpose a dose of 0.2 gram (3 grains) can be given daily for a week. The blood cyanate level is then determined. This can be easily done with a small portable kit which Eli Lilly & Co. and others produce. The amount of the drug can then be increased or decreased gradually.

It may require from 0.2 gram (3 grains) to 1 gram (15 grains) daily to maintain an adequate blood cyanate level. The blood cyanate level should be checked weekly for the first month, then every two weeks for the next two months, and monthly thereafter. Therapy is sometimes discontinued during the hot summer months. A drop in blood pressure is usually noted in from three to four weeks, but occasionally it takes longer. However, relief of subjective symptoms occurs much sooner.

The drug can be prescribed as the potassium or sodium salt in the form of 0.1 or 0.2 gram (1½ or 3 grains) tablets, or in liquid form. The official Elixir of Sodium Thiocyanate N.F. contains 0.15 gram (2¼ grains) per teaspoon (4 cc.). Thiocyanate can also be prescribed in syrup of wild cherry, *viz*:

℞

Potassium thiocyanate	6.
Syr. pruni virginianae	120.
S. 1 teaspoon (3 grains) daily.	

Although the thiocyanates can produce marked symptomatic relief and can lower the systolic and diastolic pressures in about one-half the patients, complications are common. Fatigue as a complication is usually transient and disappears spontaneously, but may require a decrease in dosage for a month or so. A maculopapular rash may appear on the extremities, chest or back. This can be relieved by antihistaminic drugs, such as pyribenzamine, chlor-trimeton, *etc.* However, if exfoliative dermatitis occurs, the drug should be stopped immediately. Nervousness and irritability, pains in the feet and bones with osteoporosis, conjunctivitis and coryza, and swelling of the thyroid gland and periorbital tissues may also occur. The most serious complication is sudden death, even though the blood cyanate level has been kept within the therapeutic range.

The thiocyanates have largely been supplanted by the newer rauwolfia, veratrum and ganglionic blocking drugs. However, in some cases of hypertension with severe headache, the thiocyanates may be helpful.

Sodium nitroprusside has recently been suggested instead of the thiocyanates. However, there has been little experience with it.

Rauwolfia Serpentina.—The powdered root of rauwolfia serpentina has been used in India for many years as a sedative and more recently as a hypotensive drug. Although its mode of action is unknown, it is effective in slowly and safely lowering the blood pressure. It can be used alone or in combination with other hypotensive drugs such as the ganglionic blocking agents, veratrum viride, or hydralazine.

The following side effects are common: drowsiness, dizziness or giddiness, headache, nightmares, stuffiness of the nose and bradycardia. In addition, signs of gastrointestinal irritation such as a tendency to diarrhea, abdominal cramps, and increased appetite may occur. These side effects can be alleviated by reducing the dosage.

Rauwolfia can be prescribed in the form of the powdered root, or partially purified mixture of alkaloids, or in the form of the pure alkaloid.

Powdered Root (Raudixin).—A dose of 100 to 150 mg. is given twice daily, usually for two weeks. This is followed by 100 to 150 mg. at night only as a maintenance dose. Raudixin is supplied as 50 and 100 mg. tablets.

Partially Purified Rauwolfia Alkaloids (Rauwiloid).—The average dose is 4 mg. in the morning and at night for two weeks. This is followed by 4 mg. at night only. Rauwiloid is supplied as 2 mg. tablets.

Pure Rauwolfia Alkaloid, Reserpine (Serpasil, Reserpoid).—The average dose is 0.25 mg. in the morning and at night for two weeks. This is followed by 0.25 mg. at night only. Serpasil is supplied as 0.1 and 0.25 mg. tablets.

If side reactions occur with any of these preparations, the dose can be halved. In other cases, these doses may have to be doubled to obtain a desired hypotensive effect. If a double dose schedule is not effective, other hypotensive drugs such as veratrum can be added.

The Veratrum Viride Alkaloids.—The veratrum alkaloidal esters are obtained from the root of the veratrum viride plant. They act by blocking the afferent vagal nerve endings in the myocardium, the aortic arch and in the carotid sinus. In this way, reflex bradycardia and vasodilatation occur. In spite of the vasodilation, the cardiac output remains unchanged. Veratrum also stimulates the emetic center of the brain. This makes it difficult to prescribe. However, when veratrum is given in combination with rauwolfia, small quantities of each drug can be used with minimal side effects.

Mild side effects may include: tingling in the fingers, a feeling of warmth over the shoulders, head and neck, slight numbness around the mouth and a cool or tingling sensation in the mouth, or substernal and epigastric burning. These symptoms are not serious and it is not necessary to stop the drug. However, if larger doses are given, the following signs of toxicity may appear: nausea, vomiting, excessive slowing of the heart, tightness of the throat, and excessive salivation. These can be relieved by the sublingual administration of 1/100 grain (0.6 mg.) atropine sulfate.

Marked hypotension and collapse may also occur. This may be accompanied by shortness of breath, sighing respiration, weakness, faintness and pallor, associated with a very slow heart rate. If the patient goes into shock

this can be relieved by the intramuscular injection of 25 to 50 mg of ephedrine sulfate, or one of the other pressor amines (page 284)

Veratrum preparations should not be given to patients who have carotid sinus sensitivity, and must be used with caution in patients with angina pectoris, myocardial infarction, extensive cerebral vascular disease, or in patients receiving quinidine or digitalis preparations.

Some of the more commonly used veratrum preparations are:

Veriloid—This is a biologically standardized extract containing a mixture of esters from veratrum viride. The average daily dose of veriloid is 9 to 15 mg, given in divided dosage three to four times a day, at intervals not less than four hours, and preferably after meals. The evening dose may be 1 or 2 mg. larger than the other doses Veriloid is supplied in 2 and 3 mg tablets, scored for divided dosage It is also available in ampoules for intramuscular and intravenous use

Provell Maleate—This is a mixture of protoveratrine A and B maleates The average daily dose is 1 to 2 5 mg., given like veriloid (see above) Provell maleate is supplied as 0 5 mg tablets, cross-scored for divided dosage.

Veralba is also a mixture of protoveratrine A and B, maleates It is supplied in the form of 0 2 and 0.5 mg scored tablets. It is also available for parenteral use (see below)

Unitensen tannate contains the alkaloidal ester, cryptenamine tannate, which has recently been isolated from veratrum viride Unitensin is supplied as 2 mg tablets The average daily dose varies from 6 to 12 mg. (3 to 6 tablets).

The veratrum alkaloids can also be given subcutaneously, intramuscularly, or intravenously, for hypertensive encephalopathy, toxemias of pregnancy, or whenever the blood pressure has to be lowered quickly. Intravenous veratrum is probably the treatment of choice for hypertensive encephalopathy

The following dose schedule has been recommended for parenteral Veralba:

PRECAUTION Veralba Injection is a powerful hypotensive drug Overdosage may produce nausea, vomiting, substernal pain, bradycardia, arrhythmia, or collapse The bradycardia, unless severe and associated with marked arrhythmias, is not necessarily harmful and may be desirable in hypertension with circulatory failure Cardiac effects are promptly improved by 1/100 gr. (0 6 mg) atropine, intramuscularly or intravenously A sudden excessive hypotension with collapse is best treated with ephedrine, 3/8 gr (25 mg) or neosynephrine (phenylephrine) 1/12 gr (5 mg) intramuscularly or intravenously These drugs should be readily available

Intravenous administration of Veralba should be reserved for medical emergencies, such as hypertensive encephalopathies or eclampsia, and should be carried out in a hospital under constant professional observation There must be continuous blood pressure readings, and the pulse should be watched for slowing and evidence of gross irregularity Subjective reactions of the patient should be observed closely, especially development of nausea or emesis

Discontinue injection if gross irregularity of the pulse or emesis occurs, particularly if neither symptom was present before treatment started Because there usually will be a further drop after the injection has been discontinued, administration should be interrupted whenever blood pressure (systolic or diastolic) falls 20 mm. of mercury below starting level

Intramuscular or Subcutaneous Use

(1) Use a syringe calibrated to permit withdrawals and injections in volumes *accurately measurable to 0 1 cc*
(2) Administration must begin at a low level and be increased, with adequate intervals between injections
(3) Start with 0 6 cc (0 12 mg) to 1 2 cc (0.24 mg) injections and take the blood pressure every 15 minutes. Maximum effect can be expected between one and two hours
(4) If the desired decrease in blood pressure is not obtained, repeat in three to four hours, using 0.2 cc (04 mg) more than on the previous injection Repeat this procedure of increasing doses until the desired lowering of blood pressure occurs
(5) If the blood pressure is not above 140/90, it is inadvisable to inject Veralba to obtain a further decrease

Intravenous Procedure

(1) Draw 0 5 cc (0 1 mg) of Veralba Injection into a 10-cc syringe Dilute this to 10 cc with 5 per cent dextrose solution, suitable for intravenous injection.
   (*a*) Inject this diluted solution at the rate of 0.5 cc to 1 0 cc per minute, with continuous observation of blood pressure.
   (*b*) If blood pressure has not fallen, and no toxicity is observed after the syringe is emptied, administer another 0 1 mg , diluted to 10 cc , under the same precautions as above
(2) If the desired decrease in blood pressure is still not obtained, proceed with injections as described above (Variation in patients is such that certain *rare cases may show the desired lowering after the administration of only* 5 cc , whereas others require 20 or more cc)
(3) After blood pressure has been reduced by administration of Veralba Injection, either of two courses may be pursued
   (*a*) The effect may be maintained as long as feasible by slow intravenous *infusion For this purpose, add one-half the contents of a vial of* Veralba Injection to 500 cc of 5 per cent glucose solution The rate of administration of this diluted solution must be determined for each patient The dose is that necessary to hold blood pressure at the desired level without producing emesis. Infusion of this diluted *solution at the rate of 0 5 cc to 1 0 cc (8 to 16 drops) per minute* will usually maintain the lowered blood pressure. During the period of infusion, the patient should be under constant observation
   Warning —Rapid infusion should at no time occur while rates of flow are becoming adjusted
   (*b*) *Following initial reduction of the blood pressure, some physicians* allow it to return to a higher level (above 140/90) and again reduce it with an intravenous injection In general, maximum reduction occurs in 10 to 30 minutes after intravenous injections Blood pressure returns to the previous level in 1½ to 3 hours

Drugs Acting on the Autonomic Nervous System —In order to understand the effect of these drugs on hypertension, the following brief review of the anatomy and pharmacology of the autonomic nervous system may be of value: *Sympathetic* nerves arise from the spinal cord, reach a paravertebral ganglion, which lies close to the spinal cord, and finally innervate a peripheral cell such as a smooth muscle cell in a blood vessel, the heart, the intestines, the bronchi, *etc* *Parasympathetic* nerves arise from the brain or from the sacral area of the spinal cord, reach a ganglion which is located at a greater distance from the cord, and innervate the same type of cell.

Stimuli are normally transmitted through both sympathetic and parasympathetic ganglia by the release of acetylcholine. Acetylcholine is also elaborated at the effector cells of the parasympathetic system and stimulates them This is the reason the parasympathetic system has been called the *cholinergic* nervous system However, in the sympathetic nervous system, the majority of the post-ganglionic cells elaborate an epinephrine-like substance. For this reason the sympathetic nervous system is called *adrenergic*.

Hypertension can be treated with drugs which interfere with the action of the sympathetic nervous system on the vascular bed, because sympathetic stimulation causes the blood vessels to contract and thus raises the peripheral resistance. Such drugs can be called *sympatholytic*, because they abolish the transmission of sympathetic impulses

A true sympatholytic drug should act primarily on the motor end-plates of the blood vessel cells Since adrenaline (epinephrine) is liberated at the sympathetic motor end-plate, it is obvious that a sympatholytic drug is also an *adrenolytic* drug However, the reverse is not true Sympatholysis may not result from a drug which is adrenolytic, because adrenolysis usually requires less potency or a lower dose than sympatholysis

A sympatholytic drug can also abolish sympathetic activity by its action in the brain or in the paravertebral sympathetic ganglia However, the transmittor of sympathetic stimuli in the paravertebral ganglia is acetylcholine, which is also elaborated by the parasympathetic system. Thus, a drug which produces a sympatholytic effect by acting on the ganglion cells must also at the same time have a parasympatholytic effect. For this reason, such drugs are called *ganglionic blocking agents* rather than sympatholytic

Ganglionic Blocking Agents —The ganglionic blocking agents in current use are synthetic compounds characterized by the presence of one or more pentavalent nitrogen groups They prevent the action of acetylcholine on the cells of the paravertebral ganglia by competing with it. They therefore cause a decrease in all the sympathetic and parasympathetic functions of the ganglia, for reasons discussed above, and one or more of the following phenomena will be noted when they are used: loss of visual accommodation and partial dilatation of the pupils, partial ptosis of the eyelids, congestion of the nasal mucous membranes, reduction of salivation, tachycardia, cutaneous vasodilation with obliteration of the temperature gradient in different parts of the body, anhydrosis; reduction of bowel motility, which can lead to severe obstipation, or paralytic ileus; interference with the tone of the urinary bladder; impotence, reduction of gastric acidity, loss of temperature regulating mechanism

In addition, the peripheral resistance is decreased and the blood pressure falls, due to orthostatic hypotension

The ganglionic blocking agent most commonly used in the treatment of hypertension is the hexamethonium ion

Hexamethonium chloride (methium, bistrium, hexameton) can be given subcutaneously, intravenously or orally. The safest methods are subcutaneous and oral administration. The greatest drawback to oral use is that tolerance quickly develops, making it necessary to use massive doses.

Subcutaneous Use.— Each time the drug is given, the patient should be propped up slightly in bed The blood pressure should be taken before and one hour after each injection Since postural hypotension is likely to occur after the injection, the patient should lie flat in bed for two hours after each dose. The postural hypotension tends to become less severe as therapy continues, so that after several weeks, the patient need only to lie flat for one hour after the injection

The initial dose of hexamethonium given subcutaneously should be 0 05 to 0 1 cc of hexamethonium chloride solution (containing 25 mg. hexamethonium ion per cc.) The dose is repeated in twelve hours in order to maintain the blood pressure at the desired level.

Patients often develop tolerance quickly to the drug and it is usually necessary to raise the dosage from day to day during the first week of therapy. After that, the same dose can be given

The following daily schedule can be used for the first week of therapy. If the blood pressure does not fall after giving the drug for a twenty-four-hour period, the next higher dose can be given the following day Once the effective daily dose has been determined, it should be continued thereafter. It is always necessary to check the blood pressure before and one hour after the injection.

The following daily schedule can be used as a guide to dosage:

Daily Dose Schedule of Subcutaneous Hexamethonium

First day	0 05 cc	hexamethonium solution*	(1 25 mg	hexamethonium ion)
Second day	0 2 cc	" "	(5 mg	" "
Third day	0 5 cc	" "	(12 5 mg	" "
Fourth day	1 cc	" "	(25 mg	" "
Fifth day	1 5 cc	" "	(27 5 mg	" "
Sixth day	2 cc	" "	(50 mg	" "
Seventh day	3 cc	" "	(75 mg	" "

* The above volumes are based on use of a hexamethonium solution containing 25 mg hexamethonium ion per cc.

In many cases, a dose of 50 mg. (2 cc.) subcutaneously, twice a day, may be sufficient In some cases, it may be necessary to give 100 mg twice a day, or more Other patients may require a dose of only 2 mg.

If the blood pressure falls greatly after an injection, the head of the bed should be lowered The pillow should be removed from under the patient's head and the foot of the bed elevated with wooden blocks The lower extremities should be elevated and passively exercised while the patient is in the head-down position.

This should be done as soon as a severe hypotensive reaction is recognized, because the longer the hypotension persists, the more difficult it is to reverse it

If the above postural methods fail to restore an adequate blood pressure, vasopressor drugs such as desoxyephedrine or phenylephrine (neosynephrine) should be given intravenously. Epinephrine (adrenaline) should not be used to counteract the effect of ganglionic blocking drugs. *In addition*, one should remember that hexamethonium may increase the sensitivity of the patient to pressor agents. The greatest danger of hypotension occurs with the initial dose, when the drug is used for the first time.

If the drug is used intravenously, the rate of injection should never be more than 0.5 mg. to 1 mg. per minute.

Oral Therapy.—Oral hexamethonium is often given in combination with hydralazine (apresoline) in the following way:

First day	Hexamethonium chloride	125	mg.	every	8	hours
	(7 A.M., 3 P.M., 11 P.M.)					
Second day	" "	125	"	"	6	"
Third day	" "	250	"	"	4	"
	(7 A.M., 11 A.M., 3 P.M., 7 P.M., 11 P.M., 3 A.M.)					
Fourth day	" "	250	"	"	4	"
Fifth day	" "	375	"	"	4	"
Sixth day	" "	500	"	"	4	"
Seventh day and eighth day	" "	500	"	"	8	"
	Plus hydralazine, 25 mg. every 8 hours (see page 573)					
Ninth day	Hexamethonium chloride	500	mg.	every	4	hours
	Plus hydralazine	50	"	"	"	"
Tenth day	Hexamethonium chloride	500	"	"	"	"
	Plus hydralazine	75	"	"	"	"

At about this time, side effects, such as lassitude, anorexia, headache, weakness, swelling of the hands or face, or puffiness under the eyes may develop. These effects usually disappear in a few days.

Treatment should never be begun with hexamethonium and hydralazine simultaneously, because sudden death may occur. The use of hydralazine after hexamethonium abolishes the side effects of the hydralazine.

The patient should be given the following instructions:

1. Take your blood pressure before each dose and record it on a chart.

The patient should be taught to take his own blood pressure. However, if this is not possible, as when he is at work, he can determine if he is taking too much hexamethonium by standing still a minute or two and noticing if he begins to feel light-headed or faint.

If he feels light-headed, he should lie down or sit with his feet elevated until the feeling passes away. He should also be cautioned about getting out of bed suddenly in the morning.

a. Take a full dose of hexamethonium, if the systolic pressure is 140 mm. Hg or higher.

b. Take one-half the dose of hexamethonium, if the systolic pressure is between 130 and 140 mm. Hg.

c. Take one-fourth the dose of hexamethonium, if the systolic pressure is between 120 and 130 mm. Hg.

d. Omit the hexamethonium, if the systolic pressure is below 120 mm. Hg.

e. Do not omit the hydralazine, regardless of the blood pressure (unless it falls below 100 mm. Hg.).

2. You must not become constipated. One to 2 (five grain) tablets of cascara, or 1 ounce (30 cc.) milk of magnesia must be taken in the evening if no bowel movement occurs during the day. If the evening laxative does not work by noon the next day, take one bottle (240 cc.) of citrate of magnesia.

The patient must not be permitted to become constipated. The reason for this is that the absorption of hexamethonium from the intestinal tract

Subcutaneous Use.— Each time the drug is given, the patient should be propped up slightly in bed. The blood pressure should be taken before and one hour after each injection. Since postural hypotension is likely to occur after the injection, the patient should lie flat in bed for two hours after each dose The postural hypotension tends to become less severe as therapy continues, so that after several weeks, the patient need only to lie flat for one hour after the injection

The initial dose of hexamethonium given subcutaneously should be 0.05 to 0.1 cc of hexamethonium chloride solution (containing 25 mg. hexamethonium ion per cc.). The dose is repeated in twelve hours in order to maintain the blood pressure at the desired level

Patients often develop tolerance quickly to the drug and it is usually necessary to raise the dosage from day to day during the first week of therapy After that, the same dose can be given.

The following daily schedule can be used for the first week of therapy. If the blood pressure does not fall after giving the drug for a twenty-four-hour period, the next higher dose can be given the following day. Once the effective daily dose has been determined, it should be continued thereafter. It is always necessary to check the blood pressure before and one hour after the injection

The following daily schedule can be used as a guide to dosage:

Daily Dose Schedule of Subcutaneous Hexamethonium

First day	0 05 cc	hexamethonium solution*	(1 25 mg. hexamethonium ion)
Second day	0 2 cc	" "	(5 mg " "
Third day	0 5 cc	" "	(12 5 mg " "
Fourth day	1 cc	" "	(25 mg " "
Fifth day	1 5 cc	" "	(27 5 mg " "
Sixth day	2 cc	" "	(50 mg " "
Seventh day	3 cc	" "	(75 mg " "

* The above volumes are based on use of a hexamethonium solution containing 25 mg hexamethonium ion per cc.

In many cases, a dose of 50 mg (2 cc) subcutaneously, twice a day, may be sufficient In some cases, it may be necessary to give 100 mg. twice a day, or more Other patients may require a dose of only 2 mg.

If the blood pressure falls greatly after an injection, the head of the bed should be lowered The pillow should be removed from under the patient's head and the foot of the bed elevated with wooden blocks. The lower *extremities should be elevated and passively exercised while the patient is* in the head-down position

This should be done as soon as a severe hypotensive reaction is recognized, because the longer the hypotension persists, the more difficult it is to reverse it

If the above postural methods fail to restore an adequate blood pressure, vasopressor drugs such as desoxyephedrine or phenylephrine (neosynephrine) should be given intravenously. Epinephrine (adrenaline) should not be used to counteract the effect of ganglionic blocking drugs. In addition, one should remember that hexamethonium may increase the sensitivity of the patient to pressor agents. The greatest danger of hypotension occurs with the initial dose, when the drug is used for the first time.

Contraindications to Hexamethonium —The contraindications to hexamethonium are relative rather than absolute and are based on the pharmacological effects of the drug, particularly the peripheral vasodilation and hypotension, which can do more harm than good

For this reason, hexamethonium must not be used in uremia or in the presence of cerebral thrombosis or hemorrhage It must be used cautiously in patients with angina or healed myocardial infarction. If the patient is on a low-sodium diet, hexamethonium must also be used very carefully, since salt restriction tends to intensify the hypotensive response In such cases, it is better to have the patient take salt.

Pentolinium tartrate (pentapyrrolidinium, M & B 2050A, ansolysen) is a ganglionic blocking agent whose pharmacological and toxic actions are similar to hexamethonium However, it is about five times more potent than hexamethonium, the effect of an oral dose lasts about twelve hours instead of three hours compared to hexamethonium, it gives a more uniform response from day to day on oral administration, and it produces less drug tolerance It is supplied as 40 and 100 mg scored tablets for oral use It can also be administered subcutaneously It can be prescribed alone or in combination with rauwolfia or other hypotensive drugs

The total daily dose may vary from 60 mg to 600 or even 900 mg in refractory cases The drug is usually given three times a day, after breakfast, in midafternoon, and at bedtime It is advisable to start with a small dose of 20 mg three times a day

A suggested schedule is the following first week, 20 mg t i d ; second week, 40 mg t. i d , third week, 60 mg t i d , fourth week, 80 mg t i d.; fifth week, 100 mg t i d , sixth week, 150 mg t. i d ; seventh week, 200 mg t i d The increase in dosage should be stopped when a desirable effect is obtained

All the precautions described above for hexamethonium apply equally to pentolinium

Hydralazine (Apresoline, 1-hydrazinophthalazine) —This is a synthetic compound which has a moderate degree of adrenergic blocking (adrenolytic and sympatholytic) action However, its chief effect on the blood pressure is due to its action on the midbrain, where it blocks an excessive outflow of sympathetic vasopressor impulses. Because of its adrenergic blocking action, it causes a marked decrease in peripheral resistance, particularly in the splanchnic area and the kidneys As a result, the cardiac output increases and a tachycardia occurs along with the drop in blood pressure

Side reactions to hydralazine are common These include, mild to severe pounding or grinding occipital headache, tachycardia, palpitation, dizziness, weakness, nausea and vomiting and postural hypotension In addition, numbness and tingling of the extremities, flushing of the face, nasal congestion, lacrimation, inflammation of the conjunctiva, or otitis media may also occur. More serious reactions include urticaria and other skin rashes and drug fever Occasionally, a localized periorbital, ankle or genital edema occurs Anemia and pancytopenia have also been reported In addition, dyspnea and anginal symptoms may occur in patients with coronary artery disease.

In patients with severe hypertension or uremia, neuropsychiatric symptoms ranging from anxiety or mental depression to drowsiness or coma may occur. Drowsiness is apt to occur if the patient is receiving barbiturates or alcohol.

Hydralazine must be given cautiously to patients with angina pectoris as it can produce myocardial anoxia even without lowering the blood pressure.

Symptoms such as headache or tachycardia, palpitation and dizziness are much less frequent if the patient has first been given one of the rauwolfia preparations for several weeks. These side reactions also do not appear if treatment has been started with hexamethonium (page 571).

The most serious complication of hydralazine is the development of a febrile, arthritic condition resembling lupus erythematosus. This occurrs when doses greater than 400 mg daily are given for six or more months. This complication apparently disappears spontaneously when the drug is stopped. In its mild form, the condition is characterized by a migratory *arthralgia of the joints of the hands or wrists, elbows, shoulders or knees.* Fever may or may not be present.

Hydralazine can be started in a daily dose of 40 mg., 10 mg. being given after each meal and at bedtime. The dose can slowly be raised over a period of four weeks to 100 mg. four times a day. It can be used in combination with veratrum, rauwolfia or with hexamethonium or other ganglionic blocking agents.

Hydralazine (apresoline) is prepared in tablet form in strengths of 10, 25 and 50 mg. It can also be used intravenously when it is necessary to lower the blood pressure immediately as in cases of hypertensive encephalopathy or in toxemias of pregnancy or eclampsia.

Summary.—A simple plan of treatment of an uncomplicated case of essential hypertension is to begin with the mildest drug, *rauwolfia.* This will usually relieve symptoms such as anxiety, headache and palpitation, and will often lower the blood pressure.

If symptoms and the hypertension persist after several weeks' trial of rauwolfia, either *veratrum* (if the pulse rate is above 80) or *hydralazine* (if the pulse rate is slow) can be added to rauwolfia in gradually increasing doses. In some patients it may be necessary to use all three drugs simultaneously. Any combination of these drugs can be used.

In a case of malignant hypertension, hexamethonium or pentolinium with or without hydralazine or rauwolfia can be used.

For hypertensive encephalopathy, intravenous or intramuscular veratrum is the drug of choice.

Rauwolfia, veratrum, or hydralazine can be started on ambulatory patients. However, hexamethonium or pentolinium should only be started on patients who are hospitalized.

Treatment of Cerebral and Psychogenic Symptoms.—*I have found* potassium iodide valuable in alleviating attacks of vertigo. The usual dose is 10 drops of the saturated solution, in water or milk, 3 times daily after meals. Toxic iodide reactions include burning or soreness of the mouth and gums, salivation, coryza, cough and excess bronchial secretion, an acneiform eruption, and even fever. The drug can be continued indefinitely

or may be stopped when the symptoms disappear. Mild sedatives, such as the bromides, barbiturates, and chloral hydrate (page 305) are also valuable. Dramamine, 50 mg. several times a day may also be helpful.

Papaverine hydrochloride in large oral doses of 1 gram (15 grains) daily has been suggested for the severe headaches that are often present, but the drug in such doses may act as a hypnotic or cause excess sweating. Occasionally a severe headache can be abolished by the intravenous injection of a 2 cc. ampoule (0 5 gram) of caffeine sodium benzoate. Small doses of nicotinic acid intravenously (25 mg.) may also alleviate headache and vertigo. The nicotinic acid can also be taken orally in doses of 50 mg. several times a day.

For hypertensive encephalopathy and an epileptiform seizure, 1 gram of magnesium sulfate (5 cc of a 20 per cent solution; or 2 cc. of a 50 per cent solution, *etc*) can be injected intravenously. A phlebotomy of 500 cc. or a lumbar puncture may also be beneficial For coma and hemiplegia due to a cerebral thrombosis, I have successfully used caffeine sodium benzoate, 2 cc (0 5 gram) intramuscularly every three hours until the patient responds. There is no effective therapy for a cerebral hemorrhage.

At the present time, parenteral veratrum (page 567) is probably the drug of choice in treating hypertensive encephalopathy.

Treatment of Epistaxis.—For profuse bleeding, the nostril can be packed with gauze or preferably absorbent cotton, soaked in a 1/2000 solution of epinephrine The pack can be removed in twenty-four hours, or even left in place for three or four days Another procedure is to place oxidized cellulose gauze (Oxycel) or Gelfoam over the bleeding spot. This stops bleeding in a few minutes. The nostril is then packed with petrolatum gauze.

If the bleeding recurs, it may be necessary to cauterize the bleeding point which usually arises from Kiesselbach's area. This contains a network of capillaries which lies in the nasal septum just within the nares. A procedure that I have used successfully is the following: The bleeding is momentarily stopped by pressure with a cotton applicator, to visualize the bleeding point. A chromic acid crystal which has just been melted on the tip of a probe is then touched to the bleeding surface. The area is then neutralized with a solution of sodium bicarbonate Even if bleeding is bilateral, only one side of the septum should be cauterized at one sitting, to prevent possible perforation of the septum

Other Drug Therapy.—For hypertensive patients with petechiæ and increased capillary fragility, or with retinal hemorrhages, rutin (which has a vitamin P activity) can be given in daily doses from 80 to 300 mg. for weeks or months

Surgical Treatment—The first operations for hypertension were based on the empirical observations that the blood pressure fell when spinal anesthesia was produced with a level somewhere above the middle thoracic region. It was therefore thought that the blood pressure could be permanently lowered if the vasoconstrictor nerves supplying the vascular bed of the splanchnic region were severed. Since the splanchnic region is supplied from the sixth thoracic to the second lumbar segments the earliest operation consisted in extensive laminectomy and bilateral division of the sixth thoracic to the second lumbar anterior spinal nerves. This was soon

replaced by less formidable operations which interrupted the sympathetic pathways to the splanchnic region, by severing the paravertebral sympathetic chains. Peet uses a bilateral supradiaphragmatic splanchnicectomy, severing a long section of the *greater splanchnic nerves, and also excising* the lower thoracic ganglia, as high as the seventh thoracic Adson and Craig perform an infradiaphragmatic splanchnicectomy and ganglionectomy. Smithwick's operation consists of a two-stage combined supra- and infradiaphragmatic splanchnicectomy and ganglionectomy. The greater splanchnic nerves are removed from the celiac ganglia, and the sympathetic trunks are excised from at least the ninth dorsal to the first lumbar, or at most from the sixth dorsal to the third lumbar. One side is done first, the second side being done in about ten days. Grimson, on the other hand, performs almost a total sympathectomy.

It had also been thought that the sympathectomy would not only relieve splanchnic vasoconstriction, but also ameliorate renal ischemia, and thus decrease the production of renin and angiotonin However, kidney blood flow is not altered after the operation, and sympathectomy must be considered as a nonspecific method of treatment It is not a cure for hypertension.

Criteria for Sympathectomy —The selection of patients for sympathectomy has been arrived at by the trial-and-error method, and there are still wide differences of opinion as to which patients are suitable for operation. Various tests have been devised to determine this. For example, in the *sodium amytal test, 3 grains of sodium amytal are given orally every hour* for 3 doses, and the fall in blood pressure noted. It was originally thought that patients who responded with a marked drop in pressure, especially if the diastolic pressure fell 30 mm or more, would respond best to the operation, but this has been found not to be so. Other tests, such as the effect of intravenous sodium pentothal, the effect of spinal or high caudal block, even the effect of adrenergic blocking agents, such as dibenamine, *etc.*, have also been used

Smithwick has developed somewhat complicated criteria for operation. He believes that the patient is a poor risk if there is nitrogen retention or poor renal function, or actual or impending heart failure, or a cerebrovascular accident, or grade 3 or 4 eye grounds

Peet has used the following criteria. "A patient below fifty-four years of age; a more or less continuously elevated blood pressure, with a systolic pressure over 170 mm and a diastolic pressure above 105 mm ; a nonprotein nitrogen below 45 mg and preferably below 40 mg. per cent; a well compensated heart; and a relatively normal cerebral function. Exceptions are occasionally made, especially in the older age group and in cases with a slightly higher nonprotein nitrogen. These exceptions are generally made because of incapacitating symptoms, such as excruciating headaches, or when there is evidence of an otherwise hopeless malignant hypertension"

Results of Sympathectomy.—Symptomatic relief is marked, and headaches, nervousness, palpitation may completely disappear. However, such symptomatic relief is not necessarily related to a significant drop in blood pressure or improvement in cardiac or renal function, which, however, may also occur. Along with a lowering of the blood pressure, papilledema and

retinal exudates and hemorrhages may disappear, the heart may shrink in size and signs of heart failure may disappear, the electrocardiogram may return to normal, and renal function may improve. However, there is a tendency for the blood pressure to become elevated after a period of months, and some patients may not even develop a significant lowering of pressure. In addition, complications such as postural hypotension, loss of ejaculatory power in men (when the lumbar ganglia are severed) are not uncommon Another disadvantage of the operation is that the patients who respond poorly to the operation are those most in need of it. The operative mortality is under 5 per cent.

I have not been greatly impressed with the results of sympathectomy *and advise it only if the patient is under fifty years, has no arteriosclerotic* complications, and is doing poorly in spite of a three-month trial of the rice diet or a similar low-sodium, low-protein diet, and the use of the newer antihypertensive drugs

Other Surgical Procedures.—Recently, it has been pointed out that when unilateral renal disease is a cause of hypertension, the clinical picture is that of malignant hypertension In such cases, the diseased kidney should be removed.

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Chapter 37

ATHEROSCLEROSIS

HARDENING of the arteries, or *arteriosclerosis*, can occur in three forms:

A. *Medial Calcification (Monckeberg's Sclerosis)*.—This occurs in the peripheral arteries and is characterized by thickening and calcification of the media. This is the cause of pipe-stem and beaded peripheral arteries. Arteriosclerotic (atherosclerotic) plaques do not occur in the intima of the vessels, and the affected arteries do not become occluded.

B. *Arteriolosclerosis*.—This occurs in the arterioles of the kidneys, and other viscera. It is characterized by an obliterative endarteritis with hyperplasia, thickening and hyalinization of the intima and hypertrophy of the media.

Arteriolosclerosis is usually a complication of hypertensive heart disease. In the kidneys, it causes glomerular obstruction, tubular atrophy and interstitial fibrosis (nephrosclerosis, or so-called primary contracted kidney).

C. *Atherosclerosis*.—This is the most important type of arteriosclerosis because it is the major cause of death in this country. Atherosclerosis affects the aorta, the coronary arteries, the cerebral arteries and the large musculo-elastic arteries of the extremities.

It is characterized by subintimal infiltration of cholesterol and other lipids at points of stress in the arteries. This infiltration can be observed as small, round or oval, yellow or white, glistening, opaque, elevated thickenings of the intima, which are called atherosclerotic plaques.

Etiology.—The exact way in which cholesterol penetrates the intima to form atherosclerotic plaques is not known. Some of the theories about how or why this occurs are as follows:

1. Leary believes that cholesterol and other lipids are taken up by the reticuloendothelial system, from which cholesterol-laden foam cells (lipophages) are released into the blood stream. Here the cells come in contact with the endothelium, and because they move slowly and are relatively inert they are pushed into the intima by the force of the arterial pressure. Inside the intima, the thick internal elastic membrane acts as a barrier to hold the foam cells just within the intima. The presence of the lipophages stimulates connective tissue growth which further enmeshes them, resulting finally in atherosclerotic plaques. Eventually the lipophages break down, forming atherosclerotic abscesses. One of the reasons that cholesterol infiltration and plaque formation does not affect the smaller arteries is that the internal elastic membrane is not thick enough in these vessels to prevent the lipophages from migrating out of the subintimal area.

2. Cholesterol and other lipids may exist in the plasma in supersaturated solution, and when a disturbance of the plasma colloid equilibrium occurs,

as with excess vibration of the column of blood, it leads to the precipitation of cholesterol on the arterial intima, producing anoxia of the endothelial cells, *increased permeability*, and *infiltration and deposition of the cholesterol* beneath the intima.

3. Another factor in the development of atherosclerosis is hyperlipemia and hypercholesterolemia It is well known that precocious or excess atherosclerosis occurs in conditions with hypercholesterolemia and hyperlipemia, such as myxedema, diabetes, the nephrotic syndrome, and essential *xanthomatosis* *Dietary habits, and possibly racial characteristics may also* influence the development of atherosclerosis. Thus, the northern Chinese, and the natives of Okinawa, who subsist largely on cereals and vegetables show very little atherosclerosis.

4 The relative amount of phospholipids in the blood, which help keep cholesterol in solution, may be more important than the actual level of cholesterol. *Another factor that may also be more important than the* actual cholesterol level is the presence of an excessive quantity of *giant molecules* (containing cholesterol and other lipids) in the plasma.

The normal range of phospholipid is from 150 to 450 mg. per cent; the normal range of cholesterol is from 150 to 235 mg per cent. The normal phospholipid/cholesterol ratio is therefore from 1 to 2 In patients who have atherosclerosis, the cholesterol level rises without a corresponding rise in phospholipids, so that the ratio becomes much less than 1.

5. There may be an excessive quantity of serum lipoproteins which are atherogenic The lipoproteins in human serum may be described in terms of their flotation rate in a salt solution when studied by means of an ultracentrifuge This is described in terms of Svedberg units (S_f units) Human serums differ from one another in the number of types of lipoproteins present, and in the relative concentration of each of the various types. There seems to be some correlation between the presence of atherosclerosis and the presence of lipoproteins of the S_f 12–20 and S_f 20–100 classes. The presence of these lipoproteins may be independent of the actual serum cholesterol level However, there is a close association between obesity and the level of these lipoproteins.

6 There is some evidence that atherosclerosis is associated with a disturbance in the distribution of lipids between the alpha and beta globulins. Thus, when atherosclerosis is present, relatively little of the cholesterol is combined with the alpha globulins, and large quantities are combined with the beta globulins This is opposite to what occurs normally.

7 Atherosclerosis may be due to an increase in the size and number of chylomicrons *These are globules of neutral fat combined with cholesterol* or phospholipid. They occur in large quantities in the plasma after a fatty meal.

8. There is evidence that heredity may be an important factor in atherosclerosis. In addition, it has been found that people with predominant muscularity, compactness and "maleness"—the so-called *mesomorphic type*—are particularly prone to coronary atherosclerosis and myocardial infarction under the age of forty years.

9. The sex hormones have also been implicated in the etiology of atherosclerosis because of the fact that atherosclerosis is relatively rare in women of the childbearing age.

10 The height of the blood pressure is also important. Thus, in patients with pulmonary hypertension due to chronic pulmonary disease or advanced mitral stenosis, pulmonary atherosclerosis occurs. Similarly, phlebosclerosis of the inferior vena cava occurs in patients with long-standing venous hypertension.

11. Factors which increase endothelial permeability accentuate atherosclerosis, and factors that decrease vessel permeability, decrease atherosclerosis. Thus, thyroid hormone, idoides, and thiocyanates, which decrease endothelial permeability have been used to prevent atherosclerosis in animals which have been fed large quantities of cholesterol

Hormones, such as ACTH and cortisone, can aggravate experimental atherosclerosis

Treatment of Atherosclerosis —Since atherosclerosis sooner of later develops in patients with hypertensive heart disease, attempts should be made to prevent its occurrence, if possible, and to prevent serious complications of atherosclerosis Although methods of preventing and treating atherosclerosis are still in the experimental stage, the following procedures have been recommended·

1 *Low-cholesterol and Low-fat Diet.*—In order to prevent the absorption of even small quantities of cholesterol, the total fat content of the diet must be greatly reduced. Thus, eggs, milk and dairy products (including cheeses, ice cream), fat meat or chicken, gravies, food prepared with fat (fried food, pastries, *etc.*) should be avoided, especially if the patient has a blood cholesterol level above 200 mg per cent Vegetable fats, such as peanut oil, Nucoa,® Spry,® Crisco,® which contain long-chain fatty acids which form esters with cholesterol and which are poorly absorbed, can be used instead of animal fat. Skim milk can also be used

The following is an example of a low-fat, low-cholesterol diet (after Morrison).

General Recommendations

1 Avoid all foods high in cholesterol, such as all animal fats

2 Use vegetable fats sparingly (Plant sterols known as phytosterol and sitosterol are not absorbed by the gastrointestinal tract to any appreciable extent but a high-fat diet seems to cause a larger synthesis of cholesterol)

3 Adequate protein, 60–100 Gm daily intake

4 Carbohydrates, 250–300 Gm daily

5 Fat content, 20–25 Gm daily —cholesterol content daily range not over 75 mg

6 The use of a daily supplementary vitamin preparation containing vitamin A concentrate is recommended

Foods Permitted

Soups Bouillon, fat-free vegetable soups, vegetable broths and soups made with skimmed milk

Meat, Fish and Poultry Lean meats, broiled, roasted, baked or boiled

Eggs Egg whites as desired, not more than 2 whole eggs weekly.

Milk and Milk Products One pint or more of skimmed milk or butter milk, cheese made from skimmed milk

Vegetables All cooked or raw, especially the green and yellow vegetables rich in vitamin A, namely, beet greens, chard, spinach, carrots, kale and mustard greens

Fruits All fruits, raw, cooked, dried and canned Use citrus or tomatoes daily.

Salads. Any raw or cooked fruit or vegetable salad and gelatin salads Serve with boiled or low fat dressings such as those containing mineral oil (refined) lemon juice, spices, vinegar, ketchup, *etc*

Cereals All cooked or dry cereals, macaroni, spaghetti and rice, serve with skimmed milk

Breads Whole wheat, enriched white, rye bread or rolls, graham and soda crackers

Desserts Fruits, tapioca, cornstarch, rice, sago, junket puddings made with skimmed milk and without egg yolks, fruit whips made with egg whites, gelatin desserts, angel food cake, macaroons and egg kisses, water ices.

Concentrated Sweets Jam, jellies, marmalade, honey, molasses, maple syrup and sugar as desired, hard candies

Beverages Tea, coffee or coffee substitutes, tomato juice, fruit or vegetable juices

Foods to Be Avoided

Soups Cream soups

Meats All glandular organs, as liver, brains, kidney, sweetbreads; pork and very fat meats, fat fish, fish roe

Milk and Milk Products Whole milk, cream, Cheddar, Swiss and all rich cheese and cheese spreads, excessive butter and butter substitutes

Eggs Egg yolks

Breads Hot breads, pancakes, waffles, coffee cakes, muffins, doughnuts

Desserts Any made with cream and egg yolks, pies, frozen creams, rich cakes and cookies.

Concentrated Fats The excessive use of fats in any form, as salad dressings, olive or vegetable oils, suet, chicken or pork fat

Miscellaneous Rich gravies, olives, nuts and avocados.

*Sample Menu**†

Meal Plan		*Amount* — *Grams*	*Amount* — *Measure*
BREAKFAST			
Fruit Juice	Orange juice	200	6⅔ ounces
Cereal	Shredded wheat	30	1 biscuit
Skimmed milk	Skimmed milk	120	4 ounces
Bread	Whole wheat toast	60	2 slices
Butter substitute	Vitamin enriched margarine	10	1 square
Sugar	Sugar	15	3 teaspoons
Hot beverage	Coffee, tea, Postum		
NOON MEAL			
Soup	Skimmed milk pea soup	150	5 ounces
Meat or cheese	Cold roast lamb, lean	60	2 ounces
	mint jelly	25	1 tablespoon
Vegetables	String beans	100	¾ cup
Salad	Sliced tomato	100	1 medium
Fruit or dessert	Canned pineapple	100	1 slice
Bread	Whole wheat bread	30	1 slice
Butter substitute	Vitamin-enriched margarine	5	½ square
Hot beverage, or skimmed milk			
EVENING MEAL			
Fruit cocktail	Grapefruit cocktail	100	½ medium
Meat	Lean meats	60	2 ounces
Potato	Baked potato	150	1 medium
Vegetables	Asparagus	100	6-8 stalks
	Banana squash	100	½ cup
Salad	Fresh pear salad	100	1 medium
Salad dressing	Boiled dressing	20	1 tablespoon
Dessert	Lemon sherbet	90	¼ quart
Bread	Whole wheat bread	30	1 slice
Milk	Skimmed milk	180	¾ pint

* SPECIAL INSTRUCTIONS

Avoid oysters, caviar and other roe
Serve only lean meat or fish
Use only 2 egg yolks per week egg whites may be used as desired.
Allow 1 pint or more of skimmed or buttermilk daily
Use only skimmed milk cheese such as cottage cheese Omit rich cheese, such as cream or Cheddar
Use no animal fats such as lard and suet in cooking Unless fat in diet is decidedly restricted, olive oil, Crisco,® margarine, mayonnaise, and French dressing and other fats from vegetables and nut oils may be used occasionally as directed
Use vegetables and fruits as desired—prepared without extra butter and cream (Plant sterols known as "phytosterol" are not absorbed by the gastrointestinal tract to any extent)
Prepare tapioca, cornstarch, rice pudding and junket with skimmed milk and without egg yolk Whips may be made with gelatin or egg white; no cream
Serve jelly, jam, marmalade, honey, molasses, syrup and sugar as desired
The vegetables included in this diet are asparagus, broccoli, carrots, green beans, kale, yellow squash, pumpkin, spinach, turnip greens and other greens other vegetables—tomato (fresh, canned or juice), vegetables commonly served raw, as celery, cucumber, lettuce and cabbage, and other cooked vegetables as beets, eggplant, onions, rutabagas and cauliflower

† Approximate composition: carbohydrate, 261 Gm , protein, 87 Gm , fat, 23 Gm , calories, 1,593, calcium, 0 89 Gm , phosphorus, 1 29 Gm , iron, 120 mg , vitamin A, 9,110 I U , thiamine, 1 91 mg , riboflavin, 2 6 mg , and ascorbic acid, 212 mg

2 *Low-caloric Diet* —This is important especially if the patient is overweight The oxidative processes of the body can be further stimulated by means of a diet rich in thiamin, nicotinic acid and riboflavin. The vitamins can be prescribed in five times the maintenance dose. Small amounts of thyroid hormone have also been recommended

3 *The Use of Lipotropic Factors of the Vitamin B Complex.*—These substances such as choline, inositol and pyridoxine act to mobilize cholesterol and other lipids from the liver and other organs by decholesterolizing tissue depots of cholesterol. Choline, for example, is involved in the transformation of fat to the phospholipid lecithin Because of the effect of these substances in mobilizing fat from the liver, they are now being used to mobilize cholesterol from atherosclerotic plaques in the arteries, and to prevent the development of atherosclerosis in persons who are predisposed to hypercholesterolemia

Choline and inositol can be prescribed for this purpose. The most suitable preparation I have found is Sirnositol Solution The total daily dose of 1 5 fluid ounces (3 tablespoonfuls) provides 22 23 grams of choline gluconate and 2 25 grams of inositol Wychol Syrup of Choline and Inositol contains approximately 25 grams of choline dihydrogen citrate and 1 5 grams of inositol in three tablespoonfuls

Choline and inositol are both present in the phospholipid, lecithin, which not only has a lipotropic action, but also acts as a colloidal stabilizer of plasma cholesterol and prevents it from being precipitated on the arterial walls

Many foods are rich in lecithin. Actually, there are many lecithins, vegetable and animal, with different chemical structures However, animal foods such as eggs, butter, liver and other animal fats and organs which are rich in lecithin are also very rich in cholesterol, so that only vegetable lecithin should be eaten, if possible. Soya beans have probably the highest

concentration of lecithin, but the legumes in general have a high lecithin content, *viz*:

Milligrams Lecithin in 100 Grams of Food	
Soya beans	1480
Beans	800
Peas	830

Lecithin can also be prescribed in the form of Granulestin Granules. This consists roughly of equal parts of lecithin, cephalin and lipositol, blended with toasted wheat germ. The average dose is 2 to 3 heaping teaspoonsful (20 to 30 grams) daily at mealtime. It can be sprinkled on cereal or other foods Granulestin is supplied in 9 oz. containers.

3 *Heparin* —The intravenous use of heparin has been suggested as a means of decreasing atherosclerosis (see page 306). The reason for its use is the following: The turbidity of the serum, due to fat globules which are present after a meal (alimentary lipemia) can be reduced or "cleared" by heparin The "clearing factor" is not heparin itself, but an enzymelike material which is formed by tissues such as the heart or lung from material which resembles the serum proteins, in the presence of heparin. This "clearing factor" is able to redistribute the lipids among the serum proteins, causing the serum to be less turbid. In addition, the serum of the atherosclerotic patient shows a less pathological distribution of lipoproteins, for at least a period of hours.

4 *Estrogens* have also been used, because atherosclerosis is less common in women than in men However, when men are given large doses of estrogens, such as 0 2 mg ethinyl estradiol daily, side reactions such as gynecomastia, nausea, dizziness and a loss of libido may occur.

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Chapter 38

CORONARY ARTERY DISEASE

CORONARY artery disease may be discovered as an incidental finding at autopsy, or may be the cause of symptoms, and may be the primary cause of death. It can result from the following conditions:

1 **Coronary Atherosclerosis and Arteriosclerotic Heart Disease.**—Coronary atherosclerosis need not cause any symptoms and may be discovered *as an incidental finding at autopsy* *When it is the cause of cardiovascular* disturbances, one can describe the condition as arteriosclerotic heart disease However, many physicians incorrectly use the term, "arteriosclerotic heart disease" as a synonym for "hypertensive cardiovascular disease," or speak freely of "hypertensive and arteriosclerotic heart disease," confusing the presence of arteriosclerosis of the aorta or peripheral arteries as signs indicating that coronary atherosclerosis is also present. This may or may not be so, but the diagnosis of coronary atherosclerosis or arteriosclerotic heart disease should be made only in the presence of positive and not presumptive findings

Pathology.—The general nature of atherosclerosis is described on page 581.

Symptoms and Signs.—As I mentioned above, coronary atherosclerosis may be present without any symptoms or abnormal signs. However, it commonly produces the anginal syndrome (Chapter 16, page 294), or myocardial infarction (Chapter 39, page 593). Rarely, left-sided heart failure may be a manifestation of arteriosclerotic heart disease However, such patients give a history or show signs of angina or myocardial infarction, and there is usually additional evidence of hypertensive cardiovascular disease present. Diabetes and/or hypercholesterolemia is a common accompaniment.

Fluoroscopic and X-Ray Examination.—The heart is usually enlarged due to the presence of associated hypertensive cardiovascular disease. However, in the absence of hypertensive cardiovascular disease, it is doubtful whether coronary atherosclerosis can cause hypertrophy of the heart Atherosclerotic dilatation and tortuosity of the aorta may be present. Calcification of the coronary arteries (see page 197) may or may not be present.

Electrocardiogram—Signs of recent or old myocardial infarction (pages 597 and 598) are usually present. However, the electrocardiogram may be normal if the process of coronary atherosclerosis and coronary occlusion has been sufficiently slow and gradual so that adequate collateral coronary circulation develops In addition, with healing of a myocardial infarct, the electrocardiogram may return completely to normal.

Diagnosis.—A diagnosis of coronary atherosclerosis or arteriosclerotic heart disease can be made on the following grounds, (*a*) if angina pectoris is present and such causes as rheumatic or syphilitic heart disease, or anemia have been ruled out, (*b*) or if electrocardiographic evidence of myocardial injury or infarction is present, and such causes as trauma, pericarditis, coronary artery embolism, periarteritis nodosa, coronary arteritis or syphilis or tuberculosis of the myocardium or malignancy of the heart are absent, or if *x*-ray examination discloses calcification of the coronary arteries or a ventricular aneurism

Although coronary atherosclerosis or arteriosclerotic heart disease can cause incomplete or complete *a-v* block, or auricular fibrillation, or bundle branch block, especially left bundle branch block, or nonspecific *RS-T* deviations or *T* wave abnormalities not characteristic of myocardial injury, the presence of these abnormalities alone is not sufficient for making a diagnosis of coronary atherosclerosis or arteriosclerotic heart disease, even though the patient is elderly, and hypertension, rheumatic heart disease or syphilis is absent

Course and Prognosis.—The course and prognosis of angina pectoris is described on page 303, of myocardial infarction, on page 602 Even, if symptoms are absent, sudden death is not uncommon However, the patient may live to a ripe old age even in the presence of severe coronary atherosclerosis The prognosis in young people with diabetes is generally poor.

Treatment—The general treatment of atherosclerosis can be used (page 583) The treatment of angina pectoris is described on page 303, of myocardial infarction, on page 604 If the diagnosis of coronary atherosclerosis is made solely on the basis of electrocardiographic or *x*-ray findings, and the patient is symptomless, it may be better not to treat the atherosclerosis than to treat the condition and to produce a cardiac neurosis. However, in such cases, I suggest a salt-poor diet (page 248) and a low-caloric diet (page 250) if the patient is overweight

2. **Coronary Artery Disease Due to Syphilis.**—See page 545.

3 **Coronary Artery Disease Due to Rheumatic Fever.**—Rheumatic fever can cause a microscopic coronary arteritis, but these lesions do not cause symptoms and do not result in angina pectoris or coronary artery occlusion or myocardial infarction

4 **Coronary Artery Disease in Other Infections.**—Conditions such as pneumonia, influenza, tuberculosis and many other infections may not only cause a myocarditis but can produce a coronary arteritis. However, the lesions in the coronary arteries are without clinical significance in almost all such cases

5 **Coronary Artery Disease Due to Periarteritis Nodosa.**—See page 519

6. **Coronary Artery Disease Due to Thromboangiitis Obliterans.**—Although patients with thromboangiitis obliterans often develop coronary artery occlusion and myocardial infarction, the coronary artery occlusion is due to coronary atherosclerosis and not to thromboangiitis of the coronary arteries in almost all if not in all cases.

7. **Aneurisms of the Coronary Arteries.**—Aneurisms of the coronary arteries are rare. They may develop after periarteritis nodosa (page 519),

coronary atherosclerosis, syphilis, bacterial endocarditis, trauma, or a congenital defect in the vessel wall. *They are usually symptomless, but occlusion of the vessel may occur with myocardial infarction, or rupture may occur with hemopericardium, pericardial tamponade and death*

8 **Medial Calcification of the Coronary Arteries (Medial Coronary Sclerosis).**—This is a rare condition affecting infants or children usually under two years. The medial calcification is associated with fibroblastic proliferation of the intima which may result in complete occlusion of the coronary artery. The infant or child may die suddenly from heart failure. The etiology is unknown, and it may be a form of metastatic calcification associated with hyperactivity of the parathyroids due to renal rickets.

9. **Coronary Embolism.**—Embolism of one or more of the coronary arteries is rare It may occur during the course of bacterial endocarditis, the lumen being occluded by a valve vegetation which has broken loose; and the characteristic clinical picture of myocardial infarction may result. Bacterial emboli to the coronary arteries on the other hand, may cause miliary myocardial abscesses, but not coronary artery occlusion and myocardial infarction

Other sources of coronary embolism are mural thrombi in the left auricle or ventricle, or pulmonary veins, or fragments of an atherosclerotic plaque at the root of the aorta. Fat embolism of the coronary arteries may also occur (page 624). The coronary arteries may also be occluded by way of a paradoxical embolism (page 392) or by arterial air embolism.

Arterial Air Embolism.—In arterial air embolism, air enters the pulmonary veins and is carried to the left auricle and the systemic circulation This is in contrast to venous air embolism where air enters a systemic vein and is carried to the right heart and to the lungs (page 625).

Air can enter the pulmonary veins accidentally if one of the pulmonary veins is pierced during thoracic surgery or pneumothorax procedures Air can enter the pulmonary veins indirectly during a thoracic procedure if the intrapleural pressure rises sufficiently to tear a pleural adhesion, which in turn produces a pleuro-venous fistula.

Symptoms and Signs.—These are due to occlusion of the *systemic arterioles* by bubbles of air, especially in the brain and heart Following the embolism, the patient feels confused A convulsive seizure often occurs with resulting monoplegia or hemiplegia or other abnormal neurological *signs which may persist for days or months. Shock* and cyanosis may develop along with Cheyne-Stokes respiration If one of the coronary vessels is blocked, marked substernal pain may develop, along *with electrocardiographic* signs of myocardial injury or infarction.

Diagnosis.—The diagnosis can usually be made from the following observations:

1. Bubbles of air can often be seen in the retinal arterioles, if ophthalmoscopic examination is done shortly after the embolism occurs Later, retinal pallor appears, and lasts several days.

2. Examination of the tongue may show sharply defined areas of pallor (Liebermeister's sign). Embolism of the skin vessels may produce marbling of the skin.

3 If a small skin incision is made over the most superior portion of the body, air bubbles will escape along with the blood (air bleeding).

Course and Prognosis.—If the amount of air aspirated into the systemic circulation is large, death will occur almost immediately. However, in other cases the patient may recover.

Treatment—There is no effective treatment. However, since air is buoyant, the patient should be kept in a head-down position to prevent cerebral embolism

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(See also pages 307 and 608)

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Chapter 39

CORONARY ARTERY DISEASE (*Continued*)
ACUTE MYOCARDIAL INFARCTION

WHAT is now described as acute myocardial infarction was for many years considered to be severe angina pectoris or status anginosus, because a typical attack of myocardial infarction shows many of the characteristics of angina pectoris However, shock is also present as well as other distinguishing features

Pathological Anatomy.—The major arterial system of the heart consists of the right and left coronary arteries and their branches The right coronary artery springs from the anterior sinus of Valsalva, just above the aortic cusp. It runs forward between the root of the pulmonary artery and the right auricle to the coronary sulcus, in which it continues downward and to the right to the inferior border of the heart. It then turns left, runs posteriorly, gives off an interventricular branch and ends by anastomosing with the circumflex branch of the left coronary artery The right coronary artery and its branches usually supply the entire right ventricle with the exception of a portion of its anterior wall In addition, they supply the right half of the posterior wall of the left ventricle, and a small strip of the interventricular septum

The left coronary artery arises from the left posterior sinus of Valsalva Its short trunk runs forward between the root of the pulmonary artery and the left auricle to the upper end of the interventricular groove where it divides into an anterior descending (interventricular) branch, and a circumflex branch The anterior descending branch continues downward in the interventricular groove toward the apex of the heart. The circumflex branch runs in the auricular-ventricular groove to the left and posteriorly. The left coronary artery and its branches supply most of the left ventricle, the small anterior portion of the right ventricle not supplied by the right coronary artery, and most of the interventricular septum

In addition to these arteries and their branches and arterioles, there are numerous additional vessels that communicate between the arteries and the cavity of the heart, or between capillaries, the Thebesian veins and the cavity of the heart, and even between the major coronary arteries However, in spite of this extremely rich anatomical blood supply, the arteries function as end-arteries, and when one is suddenly occluded, ischemia and infarction of the area supplied by it usually occurs.

The most common cause of myocardial infarction therefore is sudden occlusion of one of the major coronary arteries or its branches This can occur as a result of: (*a*) thrombotic occlusion of an artery narrowed by an arteriosclerotic plaque; (*b*) rupture of a subintimal arteriosclerotic

plaque with discharge of lipoid material into the lumen of the vessel; (c) hemorrhage into the center of an arteriosclerotic plaque, with secondary thrombosis within the lumen of the vessel, resulting in occlusion; and (d) occlusion by an embolus, as in the course of bacterial endocarditis, *etc.*, (page 508). The last method of occlusion is the least common.

If the process of occlusion is gradual, sufficient collateral circulation may develop, so that it is not uncommon to find at autopsy a completely occluded major artery without signs of myocardial infarction In other cases, diffuse fibrosis of the myocardium results, due to the fact that as the vessel slowly occludes, it causes death of scattered fibers rather than massive infarction. This is the condition that pathologists used to call "chronic myocarditis" On the other hand, if the blood supply to the heart becomes acutely inadequate, myocardial infarction can occur even if the coronary arteries remain patent. Therefore, myocardial infarction is not the same as coronary thrombosis or even coronary artery occlusion.

The gross character of the infarcted area depends on the time that elapses between the attack and death. During the first few days, the infarcted area appears deeply red, due to extravasation of blood into the muscle tissue, and to the presence of necrotic tissue The line of demarcation between infarcted and uninjured muscle appears to be very sharp, both in color and consistency, the infarcted area being soft, the softening most marked where necrosis is greatest. Although the infarct appears to lie in the center of the muscle wall, and have a triangular shape, its base nearest the endocardium, microscopic studies have shown that a small region of the subendocardial tissue remains uninjured.

Histologically, the muscle injury need not extend to the epicardial surface of the heart, but from an electrophysical point of view, one must assume that there is an injured area, surrounding the infarct, which extends to the epicardium The reason for this is that when the myocardium is injured experimentally, marked electrocardiographic changes, such as occur in myocardial infarction, only occur when the injury extends to the epicardium

Infarcts that are from four hours to five days old show marked necrosis and an acute inflammatory leucocytic reaction After two days, phagocytosis is well under way, but fibroblastic activity is not plentiful until about five days. Then, and for the next two and a half weeks, the inflammatory reaction gradually disappears, and the infarct develops a yellow mottling due to connective tissue replacement. Thus, by three weeks, regions of diffuse fibrosis are present, and by four or six months, a firm, fibrous scar indicates that healing is complete

Although infarction may occur in any part of the ventricles, it is customary to describe the infarct as anterior or posterior. Anterior infarcts may include the anterior and lateral walls of the left ventricle, the apex of the heart, the anterior wall of the right ventricle and a portion of the interventricular septum. Posterior infarcts may include the diaphragmatic and basal walls of the left ventricle and the posterior portion of the interventricular septum. Further division of the infarct into antero-septal, lateral, postero-lateral, *etc.*, is sometimes made on the basis of electrocardiographic findings. Infarction of the right ventricle is extremely rare except when the infarct extends through the interventricular septum from the left ventricle.

Etiology.—The cause of coronary artery disease, angina pectoris and myocardial infarction is not definitely known. Pathological findings in the coronary arteries are found frequently in cases of long-standing hypertension, and especially in diabetics, and others and I have found that patients who have had myocardial infarcts frequently show abnormal glucose tolerance test responses even though there are no frank signs of diabetes. In addition, hypercholesterolemia or frank diabetes are common accompaniments of coronary artery disease. Polycythemia or myxedema are occasionally etiological factors in the production of myocardial infarction. Coronary artery embolism has already been mentioned. Rarely, periarteritis nodosa, or coronary arteritis due to other conditions, or trauma may also cause myocardial infarction.

Myocardial infarction can also occur postoperatively due to shock. In such cases, pain is usually not present. Instead the clinical picture is usually persistant hypotension, dyspnea, or the development of arrythmias

Myocardial infarction frequently strikes stocky, aggressive professional or business men, but it also occurs with high frequency among manual laborers Men are affected more than women, who frequently show either diabetes or long-standing hypertension It is more common in white people than in Negroes Formerly a disease of middle age, it is now striking young people in the thirties, twenties and even the teens with greater and greater frequency. Actually no age is immune, and myocardial infarction has even been reported in infants.

There is some evidence that gout and myocardial infarction are related

Symptoms and Signs—The onset is acute with anginal-like pain, but unlike ordinary angina, there is excruciating pressure in the chest or a premonition of impending doom, and if the patient has previously suffered from angina, he quickly becomes aware that something terrible is happening Again, unlike ordinary angina, the attack of myocardial infarction usually occurs at rest, often in the early hours of the morning. Nitroglycerin brings no relief, and may make the patient worse, and even morphine may fail to bring relief. The pain which may wax and wane may last hours and even days. Nausea and vomiting are frequent accompaniments of the pain, and may persist, especially if morphine is given

Shock (page 283) of varying degree is usually present. The patient is cold, pale, his skin ashen-gray, with profuse perspiration which drenches the bedclothes The patient usually remains conscious, but he may be restless, confused, excited, or even unconscious. Hemiplegia may occur due to the decreased cardiac output and cerebral anoxia.

The pulse is usually rapid and of poor volume, unless a-v block is present when it may be slow. Irregularity of the pulse may be due to arrhythmias such as incomplete a-v block or a-v dissociation with interference, auricular nodal or ventricular premature contractions, auricular, nodal or ventricular tachycardia, or auricular flutter or fibrillation.

The blood pressure usually falls dramatically, and the systolic pressure may be 80 mm or less. A transient rise in blood pressure has been reported by some, but I have never observed this Occasionally the pressure

mains comparatively high and falls slowly over a period of hours or days. The heart sounds are distant and sometimes inaudible. A gallop rhythm may be present, but more frequently there is embryocardia, the sounds having a tic-tac quality. There is no orthopnea, and the lungs are usually clear but a few moist basal rales may be present. The abdomen may be soft but there may be epigastric and right upper quadrant tenderness and even rigidity Slight enlargement of the liver is sometimes noticeable. There is no edema

Within a few hours the shock usually begins to clear although it may persist for one or more days The pain also tends to ebb. In the majority of cases, fever quickly develops even within a few hours. (Because of the presence of shock, rectal temperatures should be taken) The temperature rises for a few days, even to 102° or higher, and falls slowly returning to normal by the end of a week However, there may be no rise in temperature at all

A pericardial friction rub is occasionally found during this early stage. It is usually transient and is due to a localized pericardial reaction over the infarct Less frequently a generalized sero-fibrinous pericarditis may occur, rarely, marked pericardial effusion occurs Irritation of the diaphragm by the pericarditis may result in hiccup

Atypical Features.—Although cases of acute myocardial infarction without pain have been reported, this is unusual. However, in some cases, the pain is minimal, the patient noticing only moderate substernal burning or a substernal boring sensation or a "lump" in the chest

Signs of shock may be absent, whereas in some cases, the clinical picture is predominantly that of shock. Occasionally, the patient presents the classical picture of acute left-sided heart failure and pulmonary edema This occurs especially in patients who have had a previously damaged heart. In such cases, the fall in blood pressure with the onset of the pulmonary edema is itself suspicious of a myocardial infarct (see page 199)

Rarely, abdominal signs are so marked that one's attention is drawn away from the heart, the attack simulating a ruptured peptic ulcer, acute cholecystitis or a gallbladder colic Cases of acute myocardial infarction have been described where, in addition to epigastric pain, there was tenderness and rigidity of the upper abdomen and slight jaundice as well as fever and leucocytosis

Premonitory Signs.—When patients who survive are questioned carefully, they frequently state that from twenty-four hours to two or even three weeks before the actual attack, their anginal pain had been becoming progressively severe and was not responding so well to nitroglycerin, or that they had begun to develop vague substernal or precordial pain, weakness, palpitation and even epigastric symptoms Whether it is possible in such cases to prevent the infarction is highly questionable It has been suggested that a patient, whose angina, for example, becomes more severe, be put to bed, for a week or so, but in my experience, infarction has occurred even when this has been done

Fluoroscopic and X-Ray Examination.—Some degree of cardiac dilatation is present, and the cardiac silhouette has a hazy outline Pulsation of the left ventricular segment is poor, and paradoxical pulsation may be present

Roentgenkymographic and electrokymographic studies will usually show a systolic expansile pulsation over the left ventricle rather than a normal systolic contractile pulsation

Electrocardiogram.—The electrocardiogram provides practically pathognomonic evidence of the infarct, when abnormal *Q* waves and *RS-T* deviations are present, and I have noted changes appearing as early as one-half

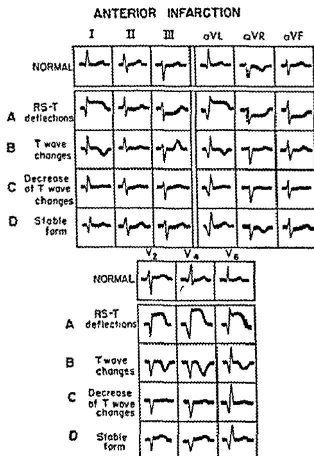


FIG 103 —The successive electrocardiographic patterns which occur after anterior infarction (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed, 1953)

an hour or an hour after the attack The general patterns of myocardial injury have already been described on page 211 Here, I shall review the progressive patterns of anterior and posterior infarction

Anterior Infarction (Fig. 103)—In a typical case of acute anterior infarction, abnormal *Q* waves and elevated, abnormal *RS-T* segments appear in one or more of the precordial leads on the left side of the chest, in lead *aVL* and usually in lead I. Occasionally, the appearance of abnormal findings

in lead I may be delayed a week or two, even though the changes are present in the other leads. Leads *aVR*, *aVF* and III show reciprocal depression of the *RS–T*. As healing takes place, the *RS–T* deviations slowly return to the base line, and deep, symmetrical *T* waves appear in the precordial leads, and leads *aVL* and I, and tall symmetrical *T* waves appear in leads *aVR*, *aVF* and III. Still later, the *T* waves shrink in size and become normal in shape, leaving only the abnormal *Q* waves in the precordial leads, and leads *aVL* and I, as signs of an old, healed myocardial infarct. However, it should be pointed out that the development of abnormal *Q* waves is not a necessary part of myocardial infarction, because abnormal *Q* waves will not appear when the infarct is small, localized and superficial.

The time relations of this sequence of progressive changes are variable, and the pattern may remain at any one stage indefinitely. For example, when a ventricular aneurysm occurs, marked deviations of the *RS–T* segment may persist for years. More commonly, the *RS–T* segments begin to return to the base line in a week or two, the progression of *T* waves continues for several months, so that by six months or a year, the tracing has returned to normal with the exception of the abnormal *Q* waves, which usually remain indefinitely

Posterior Infarction (Fig 104).—Here, the abnormal Q waves, abnormal, elevated *RS–T* segments and later, the deep symmetrical *T* waves appear in leads *aVF* and II and III. The depressed *RS–T* segments and later, the tall symmetrical *T* waves appear in leads *aVL*, *aVR*, one or more of the precordial leads and lead I The diagnosis of posterior infarction should be made from lead *aVF* or leads II and III

Subendocardial Infarction.—Occasionally, the patient shows a typical clinical picture of acute myocardial infarction with shock, but the electrocardiogram merely shows the patterns of myocardial anoxia (Fig. 62, page 297). In such cases, the myocardial infarction is limited to the subendocardial region of the left ventricle, and the zone of myocardial injury does not extend to the epicardium. The differentiation of the electrocardiographic pattern in subendocardial infarction from the pattern produced by angina pectoris and myocardial anoxia is made from serial electrocardiograms, because the *RS–T* deviations which occur in angina pectoris are transitory, whereas the *RS–T* deviations may persist for weeks or longer after subendocardial infarction As healing takes place, the *RS–T* deviations merely return to the base line without abnormal *T* waves developing.

Laboratory Tests.—With acute myocardial infarction, a marked increase in sedimentation rate occurs. This slowly returns to normal over a period of four to six weeks, but it may remain rapid much longer.

Leucocytosis occurs within a few hours after the attack, and persists for about a week The count is usually from 12,000 to 15,000 but may be as high as 25,000.

During the period of shock, there is oliguria, sometimes anuria and even nitrogen retention in the blood. In addition, transient glycosuria may occur. Several explanations for this have been proposed. I believe that it is a sign of latent diabetes, aggravated by the attack.

Diagnosis.—Common conditions that may simulate acute myocardial infarction are acute abdominal conditions, acute nonspecific or benign

pericarditis, dissecting aneurism of the aorta, spontaneous mediastinal emphysema, massive pulmonary embolism, a severe anginal attack.

Acute Abdominal Condition.—Because epigastric pain, vomiting and upper abdominal tenderness, rigidity, shock and even slight jaundice may occur, an attack of myocardial infarction can easily be mistaken for a ruptured peptic ulcer, acute cholecystitis, gallbladder colic, acute pancreatitis, and

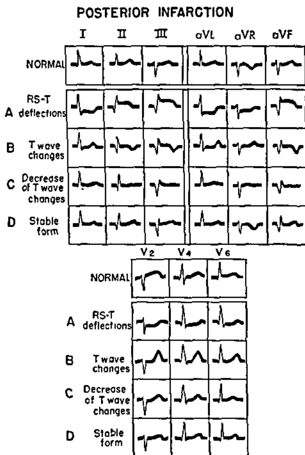


FIG 104 —The successive electrocardiographic patterns which occur after posterior infarction (From Goldberger, Unipolar Lead Electrocardiography and Vectorcardiography, Lea & Febiger, 3rd ed, 1953)

other acute abdominal conditions. However, in myocardial infarction, the cardiac findings, namely, the distance heart sounds, embryocardia or gallop rhythm, the frequent occurrence of arrhythmias, pericardial friction rub, the nature of the pain being substernal or precordial as well as epigastric, with anginal radiation, and the characteristic electrocardiographic findings enable one to make the diagnosis

Acute Nonspecific Pericarditis—Although the onset of acute nonspecific pericarditis may be as severe as an attack of myocardial infarction, including intense precordial pain and shock, fever is maximal on the first day, when a loud friction rub can also be heard, unlike cases of myocardial infarction where the peak of temperature is delayed for several days and a friction rub is delayed and transient. In addition, patients with the pericarditis frequently give a history of an upper respiratory infection a week or so before the attack

The electrocardiogram is extremely helpful With pericarditis, diffuse superficial myocardial injury usually occurs, unlike the massive localized injury of infarction. Thus, the electrocardiogram in pericarditis usually shows elevation of the *RS–T* segments in the precordial leads, leads *aVL* and *aVF* and in the three standard leads, without abnormal *Q* waves. In addition the reciprocal changes in leads *aVL* and *aVF*, and in leads I and III, seen after myocardial infarction, are absent, unless only a localized area of pericarditis is present One should also remember that a generalized pericarditis may occur after myocardial infarction

Dissecting Aneurism of the Aorta.—Severe anginal-like pain and shock may occur with a dissecting aneurism, although the pain is often more generalized than that of infarction, radiating at times into the thighs. Because the dissecting column of blood may involve the spinal arteries and the arteries supplying the abdominal viscera, bizarre neurological signs, such as weakness, and paresthesias of the lower extremities may occur as well as anuria, hematuria, ileus, melena, *etc* An aortic diastolic murmur may also appear due to dysfunction of the aortic valve caused by the dissecting column of blood No characteristic electrocardiographic changes appear, but the tracing may show left ventricular hypertrophy or strain, because of the previous hypertention. However, if the dissecting column of blood occludes one of the coronary arteries, the typical electrocardiographic patterns of myocardial infarction appear.

Spontaneous Mediastinal Emphysema—The occurrence of spontaneous mediastinal emphysema is characterized by severe substernal pressure which may radiate to the back, neck, shoulders, rarely to the arms. However, there is no drop in blood pressure, no shock, no fever or constitutional reactions of any kind, and a normal electrocardiogram On auscultation, a peculiar crunching sound, usually systolic, occasionally diastolic also, is heard, due to the presence of air in the anterior mediastinum The air also causes the area of cardiac dullness to disappear on percussion An associated secondary pneumothorax, usually small and involving the left upper chest may be present. Occasionally, the air may spread to the subcutaneous tissues of the neck. Diagnosis is confirmed by lateral *x*-ray studies of the chest, which may show the air in the tissue spaces between the heart and the anterior chest wall

Massive Pulmonary Embolism.—In addition to severe substernal pain and shock which may be present, dyspnea, cyanosis and hemoptysis are common findings. In addition, a forceful pulsation of the pulmonary artery, evident both by inspection and palpation, may be present, along with a very loud pulmonary second sound, a loud blowing pulmonary systolic murmur and a to-and-fro friction rub over the pulmonary area Marked electro-

cardiographic changes may also occur, which simulate posterior myocardial infarction in the standard leads, including *RS-T* deviations and the development of a deep Q_3. However, lead *aVF* does not show an abnormal *Q* (see also page 202).

Severe Angina Pectoris.—The differentiation of severe angina pectoris from acute myocardial infarction may be difficult, especially if the patient has had a previous myocardial infarct and the electrocardiogram is not normal. However, the absence of constitutional reactions, and the absence of serial *RS-T* and *T* changes in the electrocardiogram in the course of several days rules out acute myocardial infarction. However, *RS-T* changes may occur in angina pectoris, due to myocardial anoxia (page 297), even if the tracing shows signs of an old myocardial infarct. The differentiation of angina pectoris from subendocardial infarction is described on page 598.

The Value of the Electrocardiogram in the Diagnosis of Acute Myocardial Infarction.—Using the three standard leads and one precordial lead, the diagnosis of acute myocardial infarction can be confirmed in about 86 per cent of cases. I believe that when multiple unipolar precordial leads and augmented unipolar extremity leads are used, the percentage of correct electrocardiographic diagnoses can increase to almost 100 per cent. There are several reasons why the electrocardiogram does not show signs of myocardial infarction in all cases. First, left bundle branch block, or bizarre patterns of intraventricular conduction disturbance or complete *a-v* block, may prevent abnormal *Q* waves and *RS-T* elevations from appearing. Secondly, in cases of small anterolateral infarcts, the changes in precordial leads and even in lead *aVL* may be minimal, so that additional unipolar precordial leads over the left upper thorax may be necessary. With these exceptions, the electrocardiogram should reveal signs of myocardial injury if enough leads are taken.

Actually, the electrocardiogram merely shows the presence of myocardial injury, and an unequivocal diagnosis of myocardial infarction cannot be made because abnormal *RS-T* segments may also occur in pericarditis, and even during an attack of angina pectoris. Similarly, trauma to the heart, or any process that injures the heart muscle, such as infection, metastasis to the heart, *etc.*, may cause abnormal *RS-T* elevations. However, when abnormal *RS-T* elevations are associated with abnormal *Q* waves, a diagnosis of myocardial infarction is justified. Similarly, when *abnormal RS-T elevations are localized to either the anterior or posterior* wall of the left ventricle, and leads *aVL* and *aVF* (and I and III) show reciprocal and progressive changes, a diagnosis of myocardial infarction can usually be made, even if abnormal *Q* waves are not present.

One can determine the age of the infarct in a general way by means of serial tracings, because *RS-T* deviations occur in the acute stages, and tall and deep symmetrical *T* waves develop as healing takes place. Therefore when a recent myocardial infarct is suspected and the tracing shows marked *RS-T* deviations which in a week or so begin to return to the base line, and are succeeded by large symmetrical *T* waves, one can be fairly certain that a recent infarct is present (Figs. 103, 104). On the other hand, if marked *RS-T* deviations persist over a period of months, this indicates an old infarct.

The electrocardiogram also indicates the size of the infarct in a general way, because abnormal *Q* waves appear only when a large thickness of the ventricular wall is infarcted. Similarly, a large anterior infarct may cause changes in practically all the precordial leads, whereas a small anterior infarct will cause changes in only one or two of the precordial leads.

How Soon After an Infarct Occurs Should an Electrocardiogram Be Taken?—Characteristic changes may appear within a half hour in one or more of the unipolar leads. However, in the standard leads, characteristic changes may not appear for as long as two weeks. When a patient's history and physical signs suggest that an infarct has occurred, and the tracing shows only equivocal changes, the patient should be treated as if he had an infarct, and the tracing should be repeated the next day and at the end of one week. By this time, characteristic changes will be present, if the patient has an infarct, except in those conditions noted above.

Course and Prognosis.—An attack of myocardial infarction is very serious, and the patient's family should be warned that in the first two weeks death may occur abruptly and suddenly The usual causes of death in this period are shock, ventricular fibrillation, cardiac standstill, massive pulmonary embolism, and occasionally rupture of the heart. The percentage of the patients who die in this period is variable and depends on the source of clinical material studied. For example, mortality is higher in patients in a municipal hospital than in private practice because patients are frequently brought into the hospital, moribund. The average mortality for the first two weeks is about 20 per cent. If the patient survives this period, he has an excellent chance of living ten or more years

The following factors tend to make the prognosis poor: severe and prolonged shock, fever which does not subside within a week, left-sided heart failure and pulmonary edema, gallop rhythm, pulsus alternans, embolic phenomena, paroxysmal ventricular tachycardia. Also, the prognosis is worsened in a second or third attack of myocardial infarction.

The following complications may develop during an acute myocardial infarct·

1. **Rupture of the Heart** —Rupture of the heart is uncommon in patients who are put to bed when the attack occurs It has been found frequently in patients in mental institutions, presumably because the diagnosis is overlooked unless profound shock occurs. Rupture of the heart usually takes place in the first ten or twelve days, when necrosis is marked. Death is usually sudden, due to shock or pericardial tamponade, but if the blood clot in the pericardium seals the tear in the myocardium, the patient may live hours or days, or longer.

Occasionally, the interventricular septum perforates, or a papillary muscle ruptures. The two conditions can be differentiated in the following ways:

When the septum perforates, a murmur occurs in almost all cases. It is usually systolic, has a soft quality, and is best heard in the third and fourth intercostal spaces, just to the left of the sternum. The murmur is not transmitted to the axilla. A thrill is found in over half the cases. The electrocardiogram often shows right bundle branch block in addition to the pattern of myocardial infarction. The patient develops severe right-sided heart failure.

When a papillary muscle ruptures, a systolic, occasionally a diastolic murmur occurs in about half the cases. It is usually high-pitched, and is loudest in the vicinity of the apex of the heart. A thrill does not occur. However, a pseudo-pericardial friction rub occasionally is heard. (This may be due to vibrations produced by the motion of the twisted or tangled chordæ tendineæ following rupture of the papillary muscle.) The electrocardiogram shows the pattern of myocardial infarction, but signs of bundle branch block do not develop. The patient usually develops severe acute, left-sided heart failure, or may die abruptly.

2 **Congestive Heart Failure.**—I mentioned above that there are usually some scattered moist, basal rales, but occasionally an attack of myocardial infarction is ushered in with acute left-sided heart failure. Sometimes the pulmonary congestion appears only after the patient recovers from shock. Right-sided failure with engorgement of the liver and a rise in venous pressure is much less common

3 **Disturbances of Rhythm.**—Arrhythmias, such as sinus tachycardia, auricular fibrillation or flutter, auricular, nodal, or ventricular premature contractions, auricular, nodal, or ventricular tachycardia, and various degrees of *a-v* block or *a-v* dissociation frequently occur with the onset of the attack. The most serious of these is ventricular tachycardia Bundle branch block, right or left, transient or permanent, may also appear. Sudden death is common, especially in the first two weeks, and is due to ventricular fibrillation or cardiac standstill

4 **Thromboembolic Episodes.**—Myocardial infarction promotes stagnation of blood in the lower extremities and the development of phlebothrombosis and thrombophlebitis because of the marked decrease in cardiac output which is present, and because the patient is placed under absolute bed rest This is further accentuated if the patient suffers from varicose veins. When the thrombi form they can be easily broken off by straining at the stool, vomiting, coughing, *etc*, resulting in pulmonary embolization and *infarction, and even instantaneous death if one of the large pulmonary* arteries becomes occluded.

Other sources of emboli are mural thrombi in the cavity of either the right or left ventricle, usually at the endocardial site of the infarct. (Thrombi in the right ventricle can occur if the interventricular septum is infarcted) Thrombi can also form in the left or right auricle, if auricular infarction is also present. When these thrombi break off, both pulmonary and systemic embolization may occur, resulting in emboli in the lungs, brain, spleen kidneys, intestines, upper and lower extremities, *etc.* Such emboli can prove fatal.

In rare cases, fragments of an intracardiac thrombus, due to an *old* myocardial infarct, can cause multiple emboli throughout the systemic circulation

5. **Aneurism of the Left Ventricle.**—Aneurism of the left ventricle occurs after healing takes place, especially if the infarct was massive in size or if multiple infarcts had occurred. It can be diagnosed by physical signs (page 154) or by *x*-ray examination (page 183).

6. **The Shoulder-Hand Syndrome (Reflex Dystrophy of the Upper Extremities).**—This condition usually develops from three to twelve weeks after

the myocardial infarct, but may develop earlier or later. There may be simple fibrositis of the left or right shoulder with pain and limitation of motion, or a "frozen shoulder." The hand may also be involved with a painful, warm, purplish swelling. Later, as the swelling disappears, the hand becomes cold but the muscle may become atrophic, the tendons and palmar fascia thickened, osteoporosis of the bones may develop, and finally, a claw hand, cold, stiff, contracted and immobile, may develop. Trophic ulcers of the hand may also occur.

The cause of this condition is obscure. Disuse of the upper extremities while the patient is in bed with exacerbation of previous shoulder pathology may be the cause in some patients. According to recent work, the myocardial infarction causes a disturbance of the sympathetic innervation of the heart, which in turn sets off abnormal stimuli which are carried to the sympathetic ganglia, into the spinal cord and into the internuncial pool From here, the stimuli may travel upward into the anterior horn cells, causing disability of the shoulder, or downward into the lateral horn cells or into the sympathetics which innervate the entire upper extremity.

Treatment of the shoulder-hand syndrome is usually successful if started early I have found passive and active motion to the shoulder and upper extremity valuable in promoting normal muscle function and in breaking up adhesions

Procaine block of the stellate ganglion has also been used successfully. However, it may be necessary to give from 1 to 14 blocks, at two to seven day intervals in order to obtain improvement

Similar good results can be obtained with oral cortisone (page 495) given for about three weeks

Treatment.—The immediate problem of therapy is to combat the severe pain and shock If possible, the patient should not be removed to a hospital during this stage, if the attack occurred at home. He should be carried to bed and given morphine, atropine and oxygen I usually give one injection of morphine sulfate, 15 mg (gr $\frac{1}{4}$) and atropine sulfate, 0 4 mg. (gr $\frac{1}{150}$) intramuscularly, and immediately start oxygen therapy, using 70 to 100 per cent concentration, with a mask. The oxygen can be used continuously for the first six or even twelve hours. Then it can be used at intervals, depending on the patient's color It is often remarkable how the patient's color improves after the oxygen has been inhaled for only a few minutes The oxygen is also of great value in alleviating pain, if given in 100 per cent concentration. I try to use as little morphine as possible, because of its undesirable side-effects, namely, a tendency to aggravate vomiting, and the production of severe obstipation It may also be a factor in causing the anuria that sometimes appears. Rarely, the pain is so intense that intravenous morphine is necessary. This can be given in a dose of 4 to 5 mg ($\frac{1}{16}$ to $\frac{1}{12}$ grain).

With these procedures the shock tends to disappear in several hours However, if the shock appears to deepen or if the systolic pressure drops to 80 mm. or less, more active measures should be used (page 284).

Epinephrine should not be used to combat the shock of acute myocardial infarction, because it may increase the work of the heart and cause sudden death. Similarly, nitroglycerin is also contraindicated in the acute stage

of myocardial infarction, because it causes generalized vasodilation and can aggravate shock.

If paroxysmal auricular fibrillation or any paroxysmal tachycardia is present with a rapid ventricular rate, measures to combat shock will be useless unless sinus rhythm is restored by quinidine (page 346) or digitalis (page 348)

If necessary, the patient can be moved to a hospital after forty-eight hours

Anticoagulant Therapy.—Once the acute stage of shock is past, therapy is directed to the avoidance of complications, the most important of which are thromboembolic episodes. I use the following anticoagulant regimen

Dicumarol is given routinely. A prothrombin time is done immediately If the level is not spontaneously elevated, 200 mg Dicumarol are given in one dose (and repeated the next day). Forty-eight hours later, prothrombin time determination is done again The prothrombin time determination is repeated thereafter daily, and 200 mg Dicumarol are given daily until the prothrombin time is thirty seconds (assuming that the control reading is from fourteen to seventeen seconds) Doses of 50 to 100 mg. Dicumarol are given when the prothrombin time is between thirty and thirty-five seconds, and withheld when the prothrombin time rises above thirty-five seconds. It is resumed when the prothrombin time falls again to thirty seconds or less, after which the drug is given cautiously in doses of 50 to 100 mg The Dicumarol is continued for one week after the patient becomes ambulatory

If Dicumarol or any of the other anticoagulants is given properly, hemorrhage should not occur, unless the patient has a hemorrhagic tendency Any bleeding, such as from the kidneys, or from the rectum, *etc.*, can be controlled by the intravenous injection of 72 mg. of vitamin K An emulsion of vitamin K_1 oxide (mephyton) can be used instead of the vitamin K The emulsion is prepared in 1 cc ampoules, each cc containing 50 mg The emulsion must first be diluted with 5 to 7 cc. of sterile water or saline and injected slowly at a rate not exceeding 10 mg. per minute

Tromexan (ethyl biscoumacetate) is a synthetic anticoagulant of the coumarin series. It acts more rapidly than Dicumarol. Therapeutic hypoprothrombinemia usually occurs within eighteen to twenty-four hours and the prothrombin time returns to normal more quickly than with Dicumarol, usually within twenty-four to forty-eight hours

Tromexan is approximately 20 per cent as active as Dicumarol and therefore must be given in doses approximately five times greater. An initial loading dose of 1500 mg of tromexan is given orally. This is followed by a maintenance dose of from 300 to 900 mg, depending on the prothrombin time, which should be done daily

Tromexan occasionally can cause the following reactions: nausea, vomiting, diarrhea, urticaria or a macular papular rash, or dyspnea

Phenindione (danilone, P.I.D, hedulin) is another oral anticoagulant which can be used It shows its full therapeutic effect in about twenty-four hours. It is also rapidly dissipated because the prothrombin time returns to normal in from twenty-four to forty-eight hours after the drug is stopped The average initial dose is 200 mg, repeated in twelve hours

The average maintenance dose is 25 mg. twice a day. The drug colors alkaline urine orange. This should not be mistaken as hematuria. Resistance to the drug is common. It has been stated that daily prothrombin time tests are needed for only three days after the initial dose, and thereafter need be done only once a week or every two weeks. This observation needs confirmation.

Heparin.—I do not use heparin unless the patient has not received any anticoagulant therapy for several days. In such a case, the heparin is started and given along with oral Dicumarol. Daily prothrombin times are done and the heparin is discontinued when the prothrombin time rises sufficiently from the Dicumarol. This usually takes forty-eight hours. In this connection, one should remember that heparin is able to prolong the prothrombin time slightly.

There are many ways of giving heparin. One of the simplest is to use a concentrated aqueous heparin solution (100 to 200 mg. per cc.) and to inject it deep in the subcutaneous tissues of the arm or lateral thigh, or intramuscularly in the lateral thigh region, in a dose of 125 mg. twice a day. A coagulation time, done two and a half hours after the injection, should rise to about double or triple the preinjection value. If hemorrhage occurs, the heparin can be inactivated by the intravenous injection of protamine sulfate (Lilly) which is prepared in 5 cc. ampoules, which contain 50 mg. The dose of protamine should approximate the last dose of heparin.

Heparin can also be given intravenously in a dose of 50 mg. every four hours Heparin in a gelatin menstruum (depo-heparin) is also available. However, this causes great pain, and I have noticed a febrile reaction to it in several patients

It has been suggested that anticoagulant therapy should be used only for poor-risk cases of myocardial infarction, such as patients who show one of the following: 1, previous myocardial infarction, 2, intractable pain; 3, extreme degree or persistence of shock; 4, significant enlargement of the heart, 5, gallop rhythm; 6, congestive heart failure, 7, auricular fibrillation or flutter, ventricular tachycardia or intraventricular block; 8, diabetic acidosis, marked obesity, previous pulmonary embolism, varicosities in the lower extremities, thrombophlebitis (past or present), or other states predisposing to thrombosis.

However, I have seen thromboembolic complications occur in patients who were "good-risk" cases according to the above criteria. For this reason, I still believe that anticoagulant therapy should be used routinely in acute myocardial infarction.

Other Therapy.—The diet for the first few days is liquid, and consists of fruit juices and water. Thereafter, the patient is placed on a low-caloric, low-sodium, bland diet (page 248). The avoidance of the sodium ion is to prevent or decrease heart failure.

I also prescribe a nightly mild laxative, such as a tablespoon or two of milk of magnesia, and caution the patient against straining at the stool I do not like the patient to use a bed pan. Instead I have a commode placed at the side of the bed. If a commode is not available, I place the bed pan on a chair by the side of the bed and allow the patient to sit on it while having a bowel movement. I try to avoid giving enemas until four or five days have passed.

The patient is also advised to move his legs constantly during the day to decrease stagnation of blood in the lower extremities.

During this early stage, basal rales may be heard, but this itself is not an indication for digitalization. The occurrence of auricular fibrillation or flutter, or paroxysmal tachycardia also does not ordinarily require therapy, because these arrhythmias usually disappear spontaneously. However, if shock is present, the arrhythmia should be treated vigorously preferably with quinidine (page 346). Also, runs of multiple ventricular premature contractions, or ventricular tachycardia should be treated vigorously with quinidine (page 346). *A-v* block usually clears with atropine. If signs of marked left-sided or right-sided heart failure appear, the patient should be digitalized, and can be given small doses (0.5 cc.) of the mercurial diuretics.

Hiccups occasionally are a serious complication of myocardial infarction. If the usual home remedies are not effective, it may be necessary to do a unilateral or bilateral phrenic nerve crush.

The Treatment of Convalescence.—I believe in the dictum, "Out of bed early, and back to work soon." Assuming that the course of the patient has been uneventful, the patient can be allowed out of bed in about three weeks. I ambulate my patients in about two weeks. The first day out of bed, the patient usually feels weak, and so merely sits by the side of the bed for a short time. In two or three days he has regained much of his strength and is able to go to the bathroom. Although the patient is out of bed and ambulatory, I do not allow him to climb stairs for several more weeks. Therefore a patient living in an apartment house does not go into the street until about five or six weeks after the attack, unless, of course, there is an elevator in the building.

A recent modification of early ambulation of patients with acute myocardial infarction has been the "arm chair" treatment. The majority of patients can be taken out of bed and placed in a comfortable, padded arm chair during the first two days. Care must be taken that no pressure is exerted on the popliteal spaces. The patient remains in the chair until he experiences fatigue. Thus, the first day, the patient stays out of bed for one to two hours and by the end of a week he is spending the larger portion of the day in a chair.

Contraindications to the use of the arm chair treatment are 1, continuing state of shock, 2, marked debility, 3, concomitant cerebrovascular accident. High temperature, severe pain, a friction rub, a diastolic gallop, heart block, cardiac arrhythmias or the need for oxygen are not regarded as contraindications to such treatment. A concomitant procedure used is to elevate the headposts of the bed with 8 to 9 inch blocks. The patient is usually kept in the chair for three or more weeks and then allowed to walk. I have had no personal experience with the arm chair treatment, and have been very satisfied with the early ambulation schedule I described above.

I allow the patient to go back to work after three months. If possible, I try to modify working conditions, cautioning the patient against lifting or hauling or carrying heavy equipment or goods, and suggest to those working in the city that they go to work a little late and leave early to avoid the rush-hour.

There are many advantages to early ambulation. First I believe that it reduces the incidence of thromboembolic complications. Secondly, the patient is able to regain his strength much more quickly. Thirdly, and even more important, it is of great value in preventing the development of a cardiac neurosis, which can and has often proven more crippling and disabling than the actual heart disease.

The low-sodium diet need not be continued for more than a few weeks, but a salt-poor diet is continued during convalescence, and should be continued indefinitely. Since many of the patients are overweight, they should continue on a low-caloric diet. Whether or not an attempt should be made to treat the underlying coronary atherosclerosis by means of a low-fat, low-cholesterol diet and decholesterolizing agents (page 583) depends on one's point of view

Prophylaxis.—There is no definite method of preventing further attacks of the myocardial infarction, though the methods just described may be helpful in this regard Long-term anticoagulant therapy (page 618) has also been used, but it is very difficult to evaluate results.

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Chapter 40

COR PULMONALE
(PULMONARY HYPERTENSION AND PULMONARY HEART DISEASE)

Classification.—An increased peripheral resistance (of the systemic circulation) will produce hypertension and eventually left ventricular dilatation and hypertrophy. In a similar way, an increased resistance of the pulmonary arterial tree will produce pulmonary hypertension and eventually right ventricular dilatation and hypertrophy.

There are many causes for increased pulmonary resistance and pulmonary hypertension. The most common of these can be classified in the following way:

1. Cor Pulmonale (Right ventricular dilatation or hypertrophy due to disturbances occurring primarily within the pulmonary circulation)
   - A. Acute Cor Pulmonale:
     1. Massive Pulmonary Embolism, page 613
     2. Pulmonary Venous Air Embolism, page 625
     3. Fat Embolism, page 624
     4. Rupture of an Aortic Aneurism into the Pulmonary Artery, page 548
     5. Amniotic Fluid Embolism, page 625
   - B. Chronic Cor Pulmonale:
     1. Associated Primarily with Chronic Emphysema, page 627
     2. Associated Primarily with Pulmonary Fibrosis, page 632
     3. Associated Primarily with Obstruction of the Pulmonary Vascular System, page 635
2. *Pulmonary Hypertension Secondary to Conditions Outside the Pulmonary Circulation*
   - *A.* Cardiovascular Lesions Affecting the Left Side of the Heart (mitral stenosis, left-sided heart failure, *etc.*)
   - *B. Congenital Cardiovascular Lesions with A–V Shunts (patent ductus* arteriosus, the Lutembacher syndrome, the Eisenmenger complex, transposition of the aorta and pulmonary artery, pulmonary veins entering the right auricle, *etc.*)

ACUTE COR PULMONALE

Inasmuch as acute cor pulmonale is usually due to massive pulmonary *embolism, and inasmuch as massive pulmonary embolism and pulmonary* infarction are usually due to thrombophlebitis of the lower extremities, I shall first describe the clinical picture of *thrombophlebitis*, then *acute cor*

pulmonale due to massive pulmonary embolism, and finally *pulmonary infarction*

Thrombophlebitis.—*Thrombophlebitis* is an inflammation in or around a vein, with the formation of a blood clot in the vein. It is usually differentiated from a similar condition, *phlebothrombosis*, in the following way:

A. In phlebothrombosis, there is no inflammatory process in the vein wall, and the clot forms merely as a result of slowing of the blood stream, due to immobilization, or stagnation of blood, and an increased coagulability of the blood The cause of the increased coagulability is not well understood The thrombus is a red or coagulation thrombus and is similar to the clot which forms when blood is placed in a test tube. It is only loosely attached to the vessel wall and can be easily dislodged to produce a pulmonary embolism These thrombi originate in the veins of the calf muscles or in the veins on the plantar aspect of the foot, but may extend up into the deep veins of the pelvis or the thigh The loosely attached thrombus may break off spontaneously, or as a result of getting out of bed, straining at the stool, or coughing or hiccupping, *etc*. In most cases, however, there is no obvious precipitating cause In time, an inflammatory reaction (thrombophlebitis) occurs and results in a firm attachment of the thrombus to the vessel wall.

B In thrombophlebitis, an inflammatory process of the vein wall produces changes in the vascular endothelium which predispose to clotting The inflammatory process may be the result of bacterial invasion secondary to a perivenous lymphangitis, or may be caused by toxins or in other ways The thrombus is firmly attached to the vessel wall and does not break off easily However, a bland, non-inflammatory thrombus may occur proximal to the area of thrombophlebitis In addition, phlebothrombosis may be present in other veins of the same or opposite extremity

Phlebothrombosis and thrombophlebitis occur in both surgical and medical patients In surgical patients, thrombophlebitis is particularly serious after abdominal and pelvic operations, especially in patients with cancer, because fatal pulmonary embolism is common in this group of cases However, thrombophlebitis can occur after any surgical procedure.

In medical cases, thrombophlebitis is seen in patients who are confined to bed for long periods of time Thus, it is common in chronic heart failure, hemiplegia, myocardial infarction, and patients with cancer Other factors which increase the likelihood of thrombophlebitis in both medical and surgical cases are obesity, debility, polycythemia, leukemia, pernicious anemia, tobacco smoking, varicose veins of the lower extremities, *etc*.

In most of the medical and surgical cases, the usual site of the thrombophlebitis is one of the superficial or deep veins of the lower extremities However, thrombophlebitis may occur in the pelvic veins, or even in the inferior vena cava or the veins of the upper extremities (this occasionally occurs in heart failure) and may cause pulmonary embolism and infarction

In rare cases, sludging of blood, cryoglobulinemia (cold precipitable proteins), or cold hemagglutinins may also be a factor in the development of thrombophlebitis. ACTH or cortisone administration may be a cause in some cases.

Other causes of thrombophlebitis include: thromboangiitis obliterans, migrating thrombophlebitis, and thrombophlebitis due to mechanical or chemical injury (intravenous drugs, or infectious diseases)

Symptoms and Signs.—It is questionable whether phlebothrombosis can be recognized clinically. However, when thrombophlebitis occurs, the following signs and symptoms may appear.

1 Pain, usually referred to some part of the calf, and usually accompanied by local tenderness, especially on the outer posterior aspect of the lower leg

2. An increased firmness or elasticity of the leg muscles on compression.

3. Gentle palpation of the affected lower extremity may reveal an increase in temperature compared to the uninvolved leg However, if there is a thrombophlebitis of a deep vein, the skin temperature of the affected side may be lower than on the normal side, and the color of the affected leg may be whiter than the normal leg, due to reflex spasm of the arterioles

4 When passive dorsiflexion of the foot is attempted, limitation of motion may be found and pain in the calf is elicited (Homan's sign). Occasionally, calf tenderness, or tenderness of the biceps femoralis muscle can be elicited by manual compression of the muscles

5. Tenderness may appear along the course of the affected vein, which may be apparent even on inspection, as a firm reddened or thrombosed cord Occasionally the superficial veins over the tibia become dilated.

6 A slight elevation of temperature and pulse may be present, though this finding usually suggests that a pulmonary infarct has already occurred.

7. The affected calf shows a slight increase in its largest diameter, compared to the normal side. Or, slight cyanosis of the foot on the affected side may be evident when the leg is allowed to hang down from the side of the bed

Course and Prognosis.—It is impossible to determine when a pulmonary embolus will develop from a thrombophlebitis Usually, the more acutely inflamed the vein, the less is the likelihood that a fragment of the thrombus will break off However, fatal pulmonary embolism may occur from an asymptomatic thrombophlebitis.

Prophylaxis of Thrombophlebitis.—Pulmonary embolism can be prevented by preventing the development of phlebothrombosis and thrombophlebitis, and by the early recognition of these conditions when they do occur. Several methods of prophylaxis have been suggested:

1 *Early ambulation of postoperative and postpartum patients, beginning the first day.* There are many misconceptions of what early ambulation means. It is not enough to have the patient dangle the feet over the edge of the bed or to sit in a chair and have his legs dependent for hours at a time

Leithauser and his associates have recommended the following procedure of early ambulation of surgical patients:

"As soon as the patient recovers from the anesthetic, ambulation is begun, regardless of the magnitude of the operation The contraindications to this procedure are extremely few profound shock when the patient is practically pulseless, severe, uncontrolled hemorrhage, thyroid crisis, and in the final stage of a hopeless cancer or other disease, when death is imminent. At least four or more periods of walking are required on the day of operation Ambulation is most important and

of greatest value in patients who have been subjected to extensive surgical procedures, because here the dangerous reactions to trauma, which have to be counteracted by exercise, are severest. Prostration may limit the activity to only two or three steps on the first out-of-bed period, but experience has proved that the walking distance can be increased rapidly during each succeeding episode By the end of the day of operation, our patients usually are able to walk a considerable distance At first, the patient walks only a short distance from the bed, but repeats this, to and fro, on each out-of-bed period until the limit of tolerance is reached It should be emphasized that, no matter how great the urging by surgeons and nurses, patients will not overdo Constant reminders and orders to be more active are necessary, if the patients are to derive optimal benefit. Occasionally syncope occurs during the first out-of-bed period, but this happens far less frequently than it did when patients were confined for 10 or 15 days before they got out of bed Syncope is usually due to fear, and can be lessened by a positive, reassuring approach on the part of the nurse or surgeon An excellent way to rid the patient of such fear is to tell him to bend over and try to touch the floor. Repetition of this exercise a few times increases the circulation to the brain and gives the patient confidence If syncope does occur, the patient is returned to bed immediately, but within a few minutes the procedure is repeated "

If the patient must remain in bed, active movement of the lower extremities as much as possible is helpful In addition, the patient should change his position in bed throughout the day. Passive motion and massage to the lower extremities have also been recommended, but this may cause a thrombus to break free

2 *Prophylactic Postoperative Anticoagulant Therapy.*—This can be given to patients who are likely to develop thrombophlebitis, namely:

a Elderly patients, over fifty or sixty years,

b. In patients when a one-stage, major abdominal or pelvic operation, or herniorrhaphy, is to be done,

c. If the patient is suffering from a malignancy;

d If there is a history of previous thromboembolic complications;

e If marked varicose veins are present;

f. If there is a bad fracture or severe soft tissue injury of the lower extremities,

g Surgery in the presence of coronary artery disease, heart failure, or auricular fibrillation,

h. After delivery, if the mother has had previous thrombophlebitis or pulmonary embolism

Dicumarol (page 605), or tromexan (page 605) can be started by mouth *as soon as the patient is able to take it postoperatively* (The anticoagulants have even been started several days prior to operation, without any severe hemorrhage developing) The anticoagulants should be continued for a week after the patient becomes ambulatory.

Anticoagulant therapy is, however, contraindicated in the following conditions:

a. Hypoprothrombinemia due to severe hepatic disease, or vitamin K deficiency. Thus, in cases of severe, long-standing right-sided heart failure, with congestion of the liver, anticoagulant therapy must be used very cautiously, if at all

b. Vitamin C deficiency, until it is remedied.

c. Renal insufficiency, if marked There is some evidence that chronic renal disease is not necessarily a contraindication to anticoagulant therapy, unless anuria is present.

d Blood dyscrasias with bleeding tendencies.

e. Surgical and other trauma which leave large, raw, open surfaces; exposure of the brain or spinal cord; and operations in the presence of obstructive jaundice or severe liver disease.

f. Ulcerations or cancer of the gastrointestinal tract, the genitourinary tract, or other sites at which bleeding may be easily induced. Even a history of a healed duodenal or gastric ulcer is a contraindication to the use of anticoagulants.

g Subacute bacterial endocarditis.

h Pregnancy. (This has been questioned.)

i Hypertensive heart disease, especially if the blood pressure is greater than 200/110. In such cases, a tendency to hemorrhage (nasal, retinal, cerebral) is always present

j Cerebral hemorrhage or thrombosis Cerebral hemorrhage is a definite contraindication to anticoagulant therapy However, if the spinal fluid is not bloody in a case of cerebral thrombosis or embolism, anticoagulants can be used cautiously. One should remember that many patients with a cerebral thrombosis also have hypertension, which is an additional reason for caution In addition, cerebral softening and intracerebral hemorrhage can follow a cerebral thrombosis

3 Another simple method of preventing thrombophlebitis is to have the patient wear knee-length elastic stockings pre- and postoperatively.

4 Prophylactic bilateral femoral vein ligation has also been recommended instead of anticoagulant therapy However, recent observations have shown that bilateral femoral vein ligation does not prevent pulmonary embolism Therefore, it would be necessary to ligate the inferior vena cava to prevent pulmonary embolism coming from the lower extremities However, this may cause pitting edema, leg ulcers, rapid tiring of the limbs and intermittent claudication Therefore, ligation of the inferior vena cava should be considered in the prevention of pulmonary embolism only when all other measures fail.

Treatment —Once the diagnosis of thrombophlebitis is made, treatment should be prompt. The following can be done:

1 *Bed Rest* —Although it is important to keep the patient active to prevent thrombophlebitis, he should be placed in bed when thrombophlebitis develops Bed rest should be continued until the acute signs of the thrombophlebitis disappear. This usually takes a week or more

2. *Elevation of the Lower Extremities* —The lower extremities should be elevated above the level of the heart, especially if edema of the affected limb is present. The purpose of this is to help the lymph and edema fluid drain back to the heart. The simplest way of doing this is to raise the foot of the bed 8 inches, on blocks Pillows under the affected limb are usually not effective, because the knee usually gets raised above the foot. This hinders rather than helps drainage However, if the patient has peripheral arterial disease or heart failure, it may be dangerous to elevate the foot of the bed.

3 *Heat.*—Gentle, moist heat is one of the best means of relieving the painful venospasm and arteriospasm which are so often present in thrombophlebitis. It is just as effective as lumbar ganglionic block. Moist warm

packs should be applied over the entire lower extremity. At the beginning, they should be used continuously. As improvement occurs, they can be applied only intermittently, several times a day.

4. *Anticoagulant Therapy*.—Anticoagulants are valuable in the treatment of acute thrombophlebitis not only because they tend to prevent an extension of the thrombotic process, but because they seem to have a favorable action on the thrombotic process, causing signs of inflammation to subside quickly.

5. *Bilateral Femoral Vein Ligation*.—See page 617.

6. *Other Treatment*.—Dehydration should be avoided because it increases the tendency to thrombus formation.

Atropine, orally, in a dose of 0.3 mg. (1/200 grain) can also be given several times a day.

Parenteral trypsin has also been used in thrombophlebitis, but it is too early to evaluate its effects.

With recovery, a knee-length elastic bandage or stocking should be worn during waking hours for at least six months and preferably for a year or two.

Long-term Anticoagulant Therapy.—Anticoagulants can not only be used in the acute stage of thrombophlebitis or myocardial infarction and other conditions where the imminent possibility of thromboembolic complications is present, but as a means of long-term therapy, over a period of months and years, to prevent thrombosis or embolism, especially if the tendency toward these complications persists.

Long-term anticoagulant therapy has been used in the following conditions:

1. To prevent recurrent myocardial infarction, especially if thromboembolic complications are evident.
2. Persistent recurrent angina pectoris. In such cases, anticoagulant therapy is supposed to prevent a coronary thrombosis. My own experience with such cases has been disappointing.
3. Multiple arterial occlusions, if thrombosis or embolism is the cause.
4. Recurrent idiopathic thrombophlebitis.
5. Multiple embolization in a patient with rheumatic heart disease and auricular fibrillation. In such cases, I have seen good results from long-term anticoagulant therapy.

The daily dose of Dicumarol in such cases ranges from 50 to 75 mg. *Prothrombin time determinations should be done once a week, or every two weeks.* The therapy can be continued indefinitely.

Acute Cor Pulmonale Due to Massive Pulmonary Embolism.—Acute cor pulmonale consists of an acute dilatation of the right ventricle and the pulmonary artery. It is usually due to massive embolism of the main pulmonary artery or of one of its major branches, but it may also occur even when only a secondary branch of the pulmonary artery is occluded. It may also occur after fat or bone marrow embolism (page 624), pulmonary (venous) air embolism (page 625), amniotic fluid embolism (page 625), as a result of sudden rupture of an aortic aneurism into the pulmonary artery, after spontaneous pneumothorax, massive pulmonary atelectasis or extensive pneumonitis, and has even been reported as a result of pulmonary compression due to an acute exacerbation of a diaphragmatic hernia.

Experimentally it has been determined that as much as 66 per cent of the pulmonary circulation can be cut off without disturbing the systemic circulation. However, when the pulmonary circulation decreases still further as a result of occlusion of the main pulmonary artery or its main branches, or as a result of occlusion of one or more of the smaller pulmonary arteries, and if the decreased pulmonary blood flow is followed by generalized spasm of the pulmonary arterial tree, the right ventricle is unable to pump out the blood it is receiving from the systemic veins, acute right ventricular dilatation occurs in an attempt to overcome the obstruction, and signs of right-sided heart failure (dilated neck veins, engorgement of the liver, *etc.*) may appear.

Some degree of shock also appears because of the sudden drop in cardiac output. If the pulmonary obstruction is complete or almost so, death may occur almost instantaneously, but if one or more of the major branches are patent, the patient may not die. Other symptoms and signs such as tachypnea, dyspnea and cyanosis are due to the inadequate aeration of blood in the lungs.

In addition to the dilatation of the right side of the heart and of the pulmonary artery, small areas of cardiac necrosis are often found, localized to the subendocardial region, especially in the papillary muscles and interventricular septum, even though the coronary arteries are normal or patent. The exact way in which these areas of necrosis are produced is not known although it has been claimed that as a result of the pulmonary embolism, a vasoconstrictor pulmonocoronary reflex causes constriction of the coronary arteries and produces myocardial anoxemia (acute coronary insufficiency). However, it is possible that the myocardial changes occur simply as a result of shock.

Pathology.—At autopsy a large, coiled embolus is often found partly or completely occluding the main pulmonary artery or both its main branches. Occasionally only a medium-sized pulmonary artery is occluded, and in other cases, multiple emboli may be present. The comparatively thin but long thrombi which form in the veins of the lower extremities can occlude the main pulmonary artery because in the passage of a thrombus to the heart, it can curl up and become very wide. Some of these thrombi measure 30 cm. or more when uncoiled. The thrombus may be so large that it may project through the pulmonary valve into the right ventricular cavity.

Symptoms.—Numerous and varied symptoms may be present, the most common of which are tachypnea or dyspnea, and crushing precordial pain which may be identical with that produced by acute myocardial infarction. In addition, nausea and vomiting, pain in the abdomen, a chill, dizziness, mental confusion, even a convulsive seizure may occur.

Signs.—There is usually some evidence of shock (page 283). Cyanosis, which is due both to shock and to the deficient pulmonary circulation is also present. In addition, the dilated pulmonary artery produces a forceful pulsation which can be seen as well as felt in the second left intercostal space, and a loud pulmonic systolic murmur and thrill. There is also often present a rough friction rub over the pulmonary area, probably produced by the rubbing of the dilated pulmonary artery against the pericardium (page 161).

On percussion, broadening of the area of dullness occurs to the left of the sternum in the second and third intercostal spaces, due to the dilated pulmonary artery Right ventricular failure may be evident by distended neck veins, tenderness or engorgement of the liver, and the appearance of gallop rhythm.

Fluoroscopic and X-Ray Examination.—There have been very few x-ray observations of patients with acute cor pulmonale. Dilatation of the pulmonary artery has been noted as well as elevation of the diaphragm on the affected side

Electrocardiogram.—Acute cor pulmonale is usually associated with one of the following electrocardiographic patterns:

1. Electrocardiographic signs of right ventricular strain may appear. Precordial leads V_1 through V_5 or V_6 show rS and RS patterns and downward T waves In addition, lead aVR shows a Qr or QR pattern, due to marked clockwise rotation of the heart which is also present.

2 Signs of acute myocardial anoxemia (acute coronary insufficiency) may appear. A depressed RS–T segment appears in one or more of the precordial leads, in leads aVL, aVF, I, II, and sometimes in lead III. Lead aVR shows an elevated RS–T There is also a sinus tachycardia

3. The S_1Q_3 pattern of McGinn and White may appear. An S_1 develops T_2 tends to be low or inverted, and RS–T_2 may be depressed A Q_3 appears or becomes deeper and RS–T_3 may be elevated Studies of these patterns by means of unipolar extremity leads indicate that the S_1Q_3 is due to marked clockwise rotation of a vertical heart (lead aVL shows an RS type of pattern, and lead aVR shows a QR type of pattern) Although the Q_3 and elevated RS–T_3 may simulate posterior myocardial infarction, a differential diagnosis can be made from the augmented unipolar extremity leads, because lead aVF either shows no Q, or if a Q_{aVF} is present it is normal according to the criteria on page 202

In association with the S_1Q_3 pattern, signs of right ventricular strain appear in the precordial leads

4 Transient right bundle branch block may appear.

These four patterns may occur in combination

Diagnosis.—The sudden onset of severe precordial or substernal pain, shock, cyanosis and dyspnea or tachypnea, especially in a postoperative, or postpartum patient, or in a patient with thrombophlebitis, cancer, or in any elderly patient who has been confined to bed for several weeks, is suspicious of acute cor pulmonale due to massive pulmonary embolism

Acute myocardial infarction can simulate acute cor pulmonale. In such cases, examination of the heart usually reveals faint or even absent heart sounds rather than the loud pulmonary sounds and murmurs of acute cor pulmonale. Differential diagnosis is made from the electrocardiogram However, one should not forget that acute cor pulmonale due to a massive pulmonary embolism can occur in a patient suffering from acute myocardial infarction In such a case, the electrocardiogram will only show the signs of myocardial infarction.

Course and Prognosis.—Death may occur instantaneously (possibly from the development of ventricular fibrillation), or in the course of a few hours, from shock. However, 10 per cent or more of patients with acute cor pul-

monale may survive without further sequelæ. However, signs of pulmonary infarction may appear the next day. Rarely, organization and recanalization of a thrombus in one of the major arteries may lead eventually to pulmonary hypertension and chronic cor pulmonale.

In rare cases, the pulmonary embolism may cause a rise in pressure in the right ventricle sufficient to force blood through a foramen ovale and cause a right-to-left shunt. This actually is beneficial because it serves to alleviate the effects of the embolus on the circulation in the right side of the heart. Cyanosis will occur, due to the entrance of venous blood into the systemic circulation The patient usually also shows signs of shock, due to the pulmonary embolus In addition, paradoxical embolism through the patent foramen ovale may further complicate the clinical picture. Such a patient will die suddenly if a paradoxical embolus lodges in the foramen ovale and occludes the shunt.

Treatment.—The treatment of an attack of acute cor pulmonale is difficult because death may occur so quickly. A thrombus in the main pulmonary artery or at its bifurcation can be removed surgically by means of the Trendelenburg operation, but the operative mortality rate is over 90 per cent, *probably due to the fact that the operation is usually performed on* patients almost moribund

If surgical intervention is impossible, 100 per cent oxygen should be used Atropine can be given intravenously in doses of from 1 to 0.8 mg ($\frac{1}{60}$ to $\frac{1}{75}$ grain) in an attempt to abolish pulmonocoronary reflexes and to cause relaxation of the pulmonary vascular tree. The atropine can be repeated in three or four hours Papaverine intravenously in doses of 30 to 60 mg. ($\frac{1}{2}$ to 1 grain) has also been suggested, but it may cause general vasodilatation and accentuate shock. Morphine sulfate in doses of 15 mg ($\frac{1}{4}$ grain) can be used subcutaneously for pain

If the patient recovers from the acute attack, anticoagulant therapy should be begun with heparin (page 606) and one of the oral anticoagulants such as Dicumarol or tromexan (page 605) He should be kept in bed a week and advised against coughing or straining at the stool because this can precipitate another pulmonary embolus. The bowels should be kept open with mild laxatives and a commode at the side of the bed used instead of a bed pan

If the condition causing the acute cor pulmonale is not a massive embolus, but one of the other conditions mentioned above, this condition should be treated if possible.

PULMONARY INFARCTION

The lungs are so well supplied by both the pulmonary and bronchial arteries, and there are so many collateral vessels, that hemorrhagic pulmonary infarction does not occur after pulmonary embolism unless venous stasis is also present as in congestive heart failure or mitral stenosis, *etc.*; or unless both the bronchial and pulmonary arterial supply to an area is affected Another factor which determines whether a pulmonary infarct will appear is the time of onset of the pulmonary embolus, because it takes from three to forty-eight hours after embolism for signs of infarction to ap-

pear. Thus the patient may die from a massive pulmonary embolus before infarction develops.

The pulmonary embolism which precedes the pulmonary infarct usually arises in one of the veins of the lower extremities, as I mentioned above Occasionally, the original site of the thrombus is one of the deep pelvic veins, or a vein of the upper extremity. However, in mitral stenosis or tricuspid stenosis, the thrombus often originates in the cavity of the right auricle, and may originate in one of the pulmonary veins.

Symptoms.—Since the infarct extends to one of the pleural surfaces of the lungs, the irritation of the pleura may produce sharp chest pain which may radiate to the shoulder, neck or abdomen. The pain is usually worse on deep inspiration Cough and hemoptysis, either blood-streaked sputum or frank blood, commonly occur. Dyspnea may be present; if the infarct extends to the diaphragmatic surface of the pleura hiccup may be present. Occasionally, the patient has a sense of vague oppression in the chest and a premonition of death.

Signs.—Some degree of cyanosis is often present. Jaundice is relatively uncommon, but may appear (page 135) There is often a slight rise in temperature and an increase in pulse rate out of proportion to the temperature (Ordinarily the pulse rises 8 to 10 beats for every degree rise in temperature)

On examining the chest, there is often found exquisite local tenderness on percussion over the infarcted area, and moist rales and even bronchial breath sounds may be heard over the infarct, or signs of pleural effusion, which may be hemorrhagic, may be present. A moderate leucocytosis and a moderate increase in sedimentation rate may also be found

Fluoroscopic and X-Ray Examination.—If pulmonary embolism occurs without the development of a pulmonary infarct, a very characteristic *x*-ray pattern may appear, because beyond the point of occlusion there is an abrupt disappearance of vascular markings, and the ischemic (but not infarcted) lung is visible in the *x*-ray film as an area of *increased translucency* surrounding the occluded artery.

Pulmonary infarcts are recognized as round, irregular or triangular areas of increased density (Fig 105). They have no constant shape, but in all cases the surface of the infarct nearest the heart shows an irregular convex shape. The infarcts are always peripheral and are in contact with one or more pleural surfaces. This may not be evident in the *P–A* position, but can be demonstrated in the oblique positions. An early sign of pulmonary infarction is a vague, hazy clouding of the lung base, obscuring the costophrenic sinus. There may also be some elevation of the diaphragm on the affected side.

The infarct may be single, or multiple infarcts may be present. They are more common on the right side than on the left, and in the lower lobes than in the upper lobes On healing, the infarct shrinks, leaving a horizontal, linear scar. In some cases, the massive pleural effusion which occurs with the pulmonary infarct completely obscures the pulmonary signs.

Electrocardiogram.—Changes in the electrocardiogram may occur as a result of the pulmonary embolism which precedes the pulmonary infarct (page 620). However, electrocardiographic signs are frequently absent

because occlusion of a small pulmonary artery does not usually lead to marked circulatory disturbances.

Diagnosis.—It is extremely important to diagnose even a small pulmonary infarct because a small infarct is often a precursor to another large and often fatal one. Pulmonary infarction should be suspected in a postoperative or postpartum patient, or in a patient with a myocardial infarct,

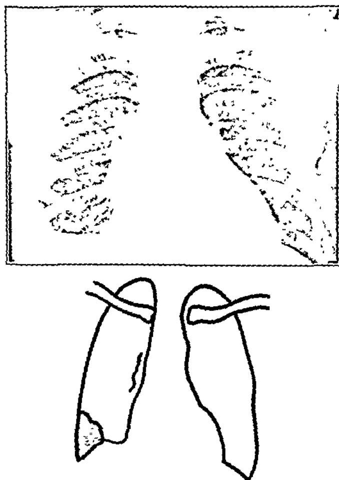


Fig. 105.—Pulmonary infarction

or in any elderly patient who has been confined to bed for more than a week, who suddenly develops a slight rise in temperature or an increase in pulse rate. Bedridden patients often give a history of "frequent attacks of pneumonia" which in all probability are due to unrecognized pulmonary infarction. In patients with myocardial infarction, the occurrence of pulmonary infarction is often misinterpreted as an extension of the myocardial infarct, and in patients with heart failure, the occurrence of multiple pul-

monary infarcts is often misinterpreted as exacerbations of heart failure. In all such patients, signs of phlebothrombosis and thrombophlebitis of the lower extremities should be sought (page 615).

Course and Prognosis.—Complete recovery usually occurs after a small pulmonary infarct. However, multiple infarcts can lead to death. Rarely, an infarct becomes infected by organisms in the upper respiratory tract, and breaks down, forming an abscess or even empyema. In other cases, multiple pulmonary emboli and infarcts may so increase the pulmonary resistance that chronic cor pulmonale develops.

Treatment. The infarct itself can be treated with penicillin to avoid secondary infection. More important, one should attempt to prevent further infarction by the prophylactic use of anticoagulants (page 616).

FAT EMBOLISM

Acute cor pulmonale due to fat embolism can result if globules of liquid fat enter the systemic veins and are carried to the lungs. Common causes of fat embolism are severe fractures or extensive crushing injuries, amputations, osteomyelitis, and even nontraumatic conditions, such as burns, phosphorus and other poisons, diabetes, *etc.* Fat embolism can also occur if ether is given intravenously for therapeutic purposes. The fat present in the plasma first dissolves in the ether and is then precipitated in the form of large globules as the ether evaporates. The amount of ether used in arm-to-lung circulation time tests is too small to produce fat embolism.

Symptoms and Signs.—The symptoms and signs of fat embolism seldom appear until at least twelve hours after an accident and rarely before the third day, but may occur much sooner. With the entrance of fat into the pulmonary circulation, the typical picture of acute cor pulmonale with sudden death may occur. In other cases, moist rales may appear in the lungs and even pulmonary edema may develop. The patient may expectorate blood-streaked sputum which contains fat, but fat in the sputum can occur in the absence of fat embolism. *X*-ray examination may reveal scattered and patchy areas of consolidation.

Since the fat globules are able to penetrate the lung capillaries and enter the systemic arterial circulation, additional symptoms may appear. Fat embolism to the brain may produce mental confusion, delirium, muscular twitching, convulsions or paralyses, involuntary passage of feces and urine, and even coma. The eye grounds may show papilledema, hemorrhages and even fat emboli. The temperature may be normal or subnormal or may rise to 106° or higher, if the heat regulating center of the medulla is disturbed. Petechial hemorrhages may appear in the skin.

Fat globules may also appear in the urine, though this may also occur in patients without fat embolism. In testing for fat in the urine, it is important to have the patient express all the urine from his bladder, because the fat is found only in the last few cc. excreted. When a platinum loop with a drop of urine on it is heated in an open flame, a characteristic popping or sizzling noise occurs as the fat is ignited.

Course and Prognosis.—Death usually occurs in from two days to about two weeks, with an average duration of life about one week. However, the patient may recover.

Treatment.—Shock should be treated with pressor substances (page 284) Oxygen can be given if there is marked cyanosis. Dehydration should be avoided.

Decholin can be given intravenously in an attempt to emulsify the fat globules. An injection of 10 cc. can be given every two hours, for even twelve or more doses Lipotropic agents (page 585) may also be helpful in emulsifying the fat globules

Bone Marrow Embolism.—Severe crushing injuries, or convulsive seizures, and in some cases, minimal trauma, may cause fragments of bone marrow to enter the venous system and produce bone marrow embolism and acute cor pulmonale. There is no effective treatment

PULMONARY (VENOUS) AIR EMBOLISM

Acute cor pulmonale can be produced if a large quantity of air enters the systemic veins and is carried to the right ventricle and the lungs. A volume of air up to 100 or 150 cc or more is usually necessary to cause death The air may remain in the right ventricle where it acts as a trap, preventing the expulsion of blood into the lungs, or it may enter the lungs and obstruct the pulmonary arterioles Unlike fat, air does not cross to the pulmonary veins and the arterial circulation Pulmonary air embolism should be differentiated from arterial air embolism (page 590).

Pulmonary air embolism can occur as a result of operations involving the neck veins, dural sinuses, or the uterine mucosa (uterine curettage), from diagnostic perirenal, peritoneal, bladder, or joint air injections, from therapeutic air lavage of the maxillary antrum, from pneumoperitoneum, from vaginal insufflation of powders, during the delivery of patients with placenta previa (the uterine veins are particularly accessible to the entrance of air, especially during pregnancy), and rarely from the accidental entrance of air during intravenous infusion Neurological operations done in the sitting position also may cause pulmonary air embolism.

Symptoms and Signs.—Cyanosis, dyspnea and shock occur suddenly, and a characteristic churning, water-wheel murmur appears over the heart, due to the presence of air in the right ventricle. The neck veins may be distended due to an increased venous pressure. Death may occur in a few minutes.

Treatment.—The patient should be turned into the left lateral position, to displace the air trapped in the outflow tract of the right ventricle. The inhalation of 100 per cent oxygen may also be helpful in causing rapid absorption of the air.

AMNIOTIC FLUID PULMONARY EMBOLISM

Pulmonary embolism caused by amniotic fluid is being recognized with increasing frequency It is characterized by sudden shock, with or without chills, during labor, in a previously normal woman It may be due to strong or tetanic uterine contractions produced by pitocin, quinine, castor

oil, or multiparity, or abnormalities of the placenta such as placenta accreta, rupture of the uterus, partial retention of the placenta, and possibly, premature marginal separation of the placenta, which would allow squamous cells and other cellular debris in the amniotic fluid to enter the uterine veins.

Death is usually ascribed to the pulmonary embolism. However, another explanation for death is anaphylaxis. Normally, amniotic fluid enters the maternal circulation and is excreted by the kidneys. This causes primary sensitization of the mother. The entrance of large amounts of amniotic fluid later, into the maternal circulation can result in anaphylaxis. Other studies have shown that the amniotic fluid can cause fibrinogenopenia and a resulting postpartum hemorrhage and death.

Treatment is expectant. Shock can be treated by vasopressor substances (page 281). Atropine, or the antihistamines may also be of some value.

CHRONIC COR PULMONALE

The following table lists the more common conditions which can cause chronic cor pulmonale. In all these conditions, one or more of the following three factors may be primarily responsible for the cor pulmonale: 1, pulmonary emphysema, 2, pulmonary fibrosis; and 3, obstruction to the pulmonary vascular system.

I. Chronic Cor Pulmonale Associated Primarily with Pulmonary Emphysema.

- A. Chronic Pulmonary Emphysema, page 627.
- B. Kyphoscoliosis, page 632.

II. Chronic Cor Pulmonale Associated Primarily with Pulmonary Fibrosis, page 632.

- A. Infectious conditions, such as tuberculosis, brucellosis, bacterial pneumonias, mycotic infections such as aspergillosis, coccidioidomycosis, actinomycosis, blastomycosis, histoplasmosis, torulosis.
- B. Toxic inhalations, such as silicosis, asbestosis, berylliosis, siderosis, bagassosis, byssinosis, fibrosis from vanadium, silver or talc, and inhalations from lipids, kerosene, *etc.*
- C. Fibrosis associated with bronchial asthma, emphysema, bronchiectasis, metastatic carcinoma to the lungs (page 635).
- D. Diffuse interstitial pulmonary fibrosis, page 635.
- E. Systemic diseases of which pulmonary fibrosis is a part, such as periarteritis nodosa, disseminated lupus erythematosus, scleroderma, fibrocystic disease of the pancreas, xanthomatosis, sarcoidosis, amyloidosis, calcinosis.

III. Chronic Cor Pulmonale Associated Primarily with Obstruction of the Pulmonary Vascular System.

- A. Multiple pulmonary emboli.
- B. Sickle cell anemia.
- C. Polycythemia vera.
- D. Schistosomiasis.

CHRONIC PULMONARY EMPHYSEMA

Chronic pulmonary emphysema (hypertrophic or obstructive emphysema) is the most frequent cause of chronic cor pulmonale This is the reason cor pulmonale has been called *emphysema heart.*

Chronic pulmonary emphysema is characterized by a loss of elasticity of the pulmonary alveoli which become distended or ruptured In the more advanced stages, there is fusion of several alveoli into one large air sac. Large alveolar blebs may also be found on the surface of the lung

Pathology —When the chest is opened post-mortem, the lungs appear to be larger than normal. They may collapse slightly, but often remain distended The bronchi may show chronic inflammation with peribronchial fibrosis Bronchiectasis of the smaller bronchi is another frequent finding Microscopically, the distended or ruptured alveolar sacs are visible. The alveolar septa show fibrosis In addition, fibrosis, narrowing and even obliteration of the capillaries are present to such an extent that the total cross section of the capillary area is greatly decreased Along with this, the pulmonary arterioles and even the larger arteries may show marked sclerotic changes

Etiology —Pulmonary emphysema can occur from any condition which causes distention of the lungs, especially if the condition interferes with expiration Normally, inspiration is accomplished by means of the active contraction of the diaphragm and the intercostal muscles. However, expiration normally is a passive act Therefore, if partial obstruction to the respiratory passageways occurs, air will pass the obstruction much more easily during inspiration than during expiration, which will be difficult, and often incomplete As a result, the lungs gradually dilate more and more

Asthma, whooping cough and chronic bronchitis are frequent causes of chronic pulmonary emphysema Less common causes are tumors in the mediastinum, or partial obstruction of the larynx Occupations such as glass blowing or playing a wind instrument may also cause emphysema In other cases, there may be an hereditary disposition. The emphysema is greatly aggravated whenever a bronchitis develops by coughing

Two other forms of emphysema may occur: 1, *Compensatory emphysema.* This results from an overstretching of normal portions of the lungs to compensate for a collapsed or diseased portion of the lung, such as occurs in pulmonary fibrosis It is a contributory cause of cor pulmonale 2, *Senile emphysema* This is secondary to an angulation of the spine due to degeneration of the intervertebral discs It does not produce cor pulmonale.

Pathological Physiology.—There are three fundamental disturbances in chronic pulmonary emphysema·

1. The flow of air in and out of the lungs is greatly obstructed This is caused by a loss of elasticity of the lungs and by bronchial spasm and edema of the mucosa, and by actual obstruction of the air passageways due to thick bronchial secretions and exudates.

Because of this, the vital capacity, and more important, the maximum breathing capacity (the maximum volume of air which can be ventilated

in a minute) are greatly diminished. In order to compensate for this, the minute volume of respiration (the volume of air that the patient actually ventilates per minute) rises above normal. Therefore the patient has to perform more work to obtain the required amount of oxygen from the inspired air For example, a patient with chronic pulmonary emphysema may have to breathe up to 35 liters or more of air in order to absorb 1 liter of oxygen, whereas a normal person might have to ventilate only 20 liters of air

2 The air is unevenly distributed to the alveoli, and the blood returning to the lungs for aeration is also unevenly distributed to the alveoli. Thus, the alveolar air contains an abnormally low oxygen content, the pulmonary capillaries do not receive an adequate amount of oxygen and the venous blood cannot give up the proper amount of carbon dioxide. As a consequence, anoxia and hypercarbia (hypercapnia, an excess of CO_2 in the blood) develop along with a high serum bicarbonate level

When this stage is reached, further circulatory complications may appear The anoxia causes an increase in pulmonary arterial pressure, probably reflexly *This increases the work of the right ventricle In addition,* the anoxia stimulates the bone marrow and a secondary polycythemia, with an increased viscosity of the blood, develops This puts a further strain on the heart

3 The distortion, obstruction and occlusion of the pulmonary capillary system which occurs as a result of the emphysema causes the resistance of the pulmonary vascular bed to rise This increases the work of the right ventricle and causes right ventricular hypertrophy in much the same way that an increased peripheral vascular resistance causes left ventricular hypertrophy in hypertensive heart disease

As a result of the above factors, chronic pulmonary emphysema causes an increased cardiac output Even when heart failure occurs and the cardiac output falls, the level of the cardiac output will be statistically above normal This is the reason that heart failure occurring in a patient with chronic pulmonary emphysema and in other cases of cor pulmonale has been called *high-output* failure (page 230) The increased cardiac output present in patients with chronic cor pulmonale is probably the reason that left ventricular hypertrophy *also* occurs, even in cases uncomplicated by systemic hypertension However, not all cases of cor pulmonale have a high cardiac output. (Another explanation for the high cardiac output in cases of cor pulmonale is that when the emphysema or the pulmonary fibrosis distorts the pulmonary vascular architecture, anastomoses develop between the pulmonary and the bronchial arteries. As a result, a condition similar to multiple arterio-venous fistulas occurs in the lungs and causes a high cardiac output see page 663.)

Symptoms. –Symptoms may be due to both pulmonary and cardiac factors. Dyspnea occurs on exertion and even at rest, along with a chronic cough and expectoration even when heart failure is absent However, when heart failure occurs, the symptoms are aggravated. In addition, when right-sided heart failure develops, right upper quadrant abdominal pain, due to congestion of the liver may appear.

Cerebral symptoms, such as fainting, vertigo or somnolence, even disorientation and paranoia may occur. These symptoms are due to cerebral anoxia and secondary polycythemia (They can be *aggravated* by oxygen therapy—see page 631).

Severe substernal pain, which resembles angina pectoris (angina hypercyanotica) may occur, especially on exertion (page 300) This is due to the fact that the resting cardiac output is so high that the heart cannot increase its output sufficiently for the needs of exercise

Signs.—Chronic pulmonary emphysema can usually be recognized by inspection The appearance of the chest shows a characteristic barrel shape, due to the marked increase in its anteroposterior diameter There is also an upper dorsal kyphosis and the chest is held in permanent inspiration, so that the shoulders appear elevated and the neck shortened. Percussion of the lungs reveals increased resonance or even tympany Breathing is usually more rapid and shallow than normal

Even in the early stages there may be moderate peripheral cyanosis of the lips or lobes of the ears, which increases on slight exertion.

However, central cyanosis of some degree, with or without clubbing, is usually present When right-sided heart failure occurs, the cyanosis may become so intense that the patient develops a purplish-black color. (In such cases, there is the added factor of peripheral cyanosis due to the right-sided failure and peripheral stagnation of blood)

The neck veins may be slightly distended even if right-sided heart failure is absent This occurs because expiration is an active process in emphysema Therefore the intrapleural pressure becomes positive during expiration instead of negative, and hinders the entrance of blood into the thorax When right-sided heart failure develops, a large liver, a positive hepato-jugular reflux (page 110), and even ascites and pleural effusion may appear Left-sided heart failure, with rales in the chest may also appear However, rales, if present, are usually due to the chronic pulmonary disease

Physical examination of the heart may not reveal many abnormal findings, and the heart may not appear to be enlarged in spite of the fact that right ventricular hypertrophy may be present anatomically The pulmonary second sound is usually accentuated and may be split, though this may also occur normally (page 41). A pulmonary systolic and rarely a pulmonary diastolic murmur may also appear due to the pulmonary artery dilatation (pages 163 and 164). A systolic pulsation may be felt to the left of the lower sternal border, due to the right ventricular hypertrophy (page 154) Sinus rhythm is usually present, usually with sinus tachycardia. Auricular fibrillation is comparatively uncommon

Fluoroscopic and X-Ray Examination.—The cardiac silhouette may appear normal in spite of the presence of right ventricular hypertrophy. The heart may appear deceptively small and pendulous (drop heart, tropfenherz), when emphysema is present. Occasionally the heart has a triangular shape Signs of left ventricular enlargement may be present The pulmonary artery segment is usually accentuated, and the hilar vessels are prominent, with forceful pulsations. In the later stages, with the development of heart failure, generalized cardiac dilatation may appear.

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As a result of the above factors, chronic pulmonary emphysema causes an increased cardiac output. Even when heart failure occurs and the cardiac output falls, the level of the cardiac output will be statistically above normal. This is the reason that heart failure occurring in a patient with chronic pulmonary emphysema and in other cases of cor pulmonale has been called *high-output* failure (page 230). The increased cardiac output present in patients with chronic cor pulmonale is probably the reason that left ventricular hypertrophy also occurs, even in cases uncomplicated by systemic hypertension. However, not all cases of cor pulmonale have a high cardiac output. (Another explanation for the high cardiac output in cases of cor pulmonale is that when the emphysema or the pulmonary fibrosis distorts the pulmonary vascular architecture, anastomoses develop between the pulmonary and the bronchial arteries. As a result, a condition similar to multiple arterio-venous fistulas occurs in the lungs and causes a high cardiac output (see page 663.)

Symptoms. Symptoms may be due to both pulmonary and cardiac factors. Dyspnea occurs on exertion and even at rest, along with a chronic cough and expectoration even when heart failure is absent. However, when heart failure occurs, the symptoms are aggravated. In addition, when right-sided heart failure develops, right upper quadrant abdominal pain, due to congestion of the liver may appear.

dioxide from the blood, and combatting any pulmonary infections and cough which may be present.

The following can be done for the patient with chronic pulmonary emphysema:

1 *Breathing Exercises.*—The patient with chronic pulmonary emphysema does not use his diaphragm in breathing Diaphragmatic breathing can be retaught by the following exercises:

(*a*) In order to learn proper diaphragmatic breathing, lie down and place one hand on your abdomen and lower ribs and the other on your chest If your abdomen protrudes as you breathe in, you are breathing with the aid of your diaphragm, *which is the correct way If your abdomen does not protrude as you breathe in, practice until you have learned to achieve diaphragmatic breathing* Then proceed to next step

(*b*) Place both hands, fingertips touching, on your abdomen below the navel, and inhale naturally During the last part of each "breathing out," *press firmly inward and upward with your hands* This helps you to get rid of the trapped air and teaches diaphragmatic breathing If you do this exercise correctly, your abdomen and diaphragm move, but the chest remains almost at rest In time, as the correct breathing becomes a habit, you may not need your hands as pressure *Practice this exercise for 2 minutes lying down, then for 2 minutes sitting up, then for 2 minutes while walking*

(*c*) Repeat Exercise (*b*) from six to twelve times a day, but plan your exercise so you will always have a 15 to 30 minute rest period before each meal Avoid fatigue

An abdominal belt may also help keep the diaphragm high

2 *Inhalations of Bronchodilators* — The inhalation of vaporized bronchodilators such as vaponephrin, norisodrine or aludrel (isuprel) is often very effective in alleviating the symptoms of cough and wheezing due to bronchial obstruction Three to eight drops of the undiluted bronchodilator solution are vaporized and inhaled, over a ten to twenty minute period, using a manually operated nebulizer (A better result can be obtained with the bronchodilator drugs if used in conjunction with a positive pressure apparatus) Such inhalations can be used three or four times a day

One should caution the patient that side effects such as dizziness, palpitation, nervousness and tachycardia can occur because the bronchial dilators are sympathomimetic amines related to epinephrine and are capable of causing an increased cardiac output and even myocardial anoxia If side effects occur, the dose should be decreased, or the inhalations stopped

Oral aminophylline (page 305), sputum liquefiers such as potassium iodide, or elixir of terpin hydrate, or steam inhalations or the inhalation of detergents such as Alevaire (Winthrop-Stearns) may also be helpful if the sputum is thick and viscid

3 *Oxygen Therapy* —Oxygen is often required when anoxia and cyanosis are marked However, oxygen can be harmful for the following reason: Normally, the respiratory center in the brain responds to carbon dioxide retention in the blood However, when the carbon dioxide content of the blood is elevated over long periods of time, the respiratory center becomes insensitive to it and responds instead to anoxia The inhalation of oxygen to such patients will alleviate the anoxia, but respiratory activity will diminish and the carbon dioxide content of the blood may rise so high that the patient may become disoriented, develop coma and die.

Therefore, in an emphysematous patient, one should always determine the carbon dioxide content of the *arterial* blood before starting oxygen therapy, and if there is retention, some mechanical means of respiration, such as a respirator should be used to maintain adequate alveolar ventilation while the oxygen is being given

(The normal carbon dioxide content in arterial blood is from 44 to 52 volumes per cent When the level rises to over 80 or 85 volumes per cent, this indicates that carbon dioxide narcosis is impending.)

4 *Other Therapy* Sedatives such as the barbiturates, codeine, morphine, demerol can further depress respiration and should not be used if the patient is acutely ill If sedation is absolutely necessary, chloral hydrate (page 305) or paraldehyde, intramuscularly, in a dose from 4 to 16 cc can be used.

It is sometimes necessary to relieve the polycythemia by means of repeated phlebotomies (page 237).

5 Heart failure is treated in the usual way with a low-sodium diet, mercurials and digitalis If polycythemia is marked, one must be careful not to cause excessive diuresis with the mercurials because hemoconcentration and thrombosis may occur Carbonic anhydrase inhibitors (page 255) may be effective.

CHRONIC PULMONARY FIBROSIS

Cor pulmonale can result from a generalized extensive pulmonary fibrosis Therefore one does not usually see it as a result of uncomplicated pulmonary tuberculosis or from localized areas of pulmonary fibrosis occurring after a lung abscess or bronchiectasis The cor pulmonale develops when the fibrosis is sufficient to distort and decrease the total cross area of the pulmonary capillary bed to such an extent that the pulmonary resistance is increased and pulmonary hypertension occurs In other words, in cases of cor pulmonale resulting from pulmonary fibrosis (see Table on page 626), anoxia is not important

Dyspnea and cough are early symptoms. The volume of sputum is small, unless there is an associated emphysema. Cyanosis, clubbing of the fingers and signs of right-sided heart failure occur when the pulmonary insufficiency is far advanced. X-ray examination reveals the marked, diffuse pulmonary fibrosis.

The treatment of cor pulmonale due to pulmonary fibrosis is *not as successful* as when it is due to emphysema, because there is not much that can be done to alleviate the pulmonary fibrosis. *However, pulmonary infections should be vigorously treated with antibiotics*, and in such conditions as Boeck's sarcoidosis and beryllium granulomatosis of the lungs, ACTH and cortisone are helpful in preventing excess fibrosis.

OTHER CLINICAL CONDITIONS ASSOCIATED WITH CHRONIC COR PULMONALE

Chronic Cor Pulmonale Due to Kyphoscoliosis.—Severe deformities of the chest and spine, such as kyphoscoliosis, and even severe kyphosis,

scoliosis or lordosis, often produce chronic cor pulmonale in a manner similar to that which occurs in chronic pulmonary disease. Because of the thoracic distortion, secondary changes in the lung appear, including atelectasis and fibrosis of the compressed lung, (with emphysema on the other side), bronchiectasis, and even chronic pneumonitis. There also occurs marked reductions in lung volume, in vital capacity and maximum breathing capacity, and a compensatory increase in the minute volume of respiration. In addition, torsion and rotation of the heart may cause kinking of the pulmonary artery or its main branches, and thus interfere with the flow of blood from the right ventricle.

Symptoms.—Dyspnea is common and may be severe because of the distortion and rigidity of the thoracic cage. It tends to become more marked after adolescence with the arrest of skeletal growth. In addition, the patient often complains of marked weakness and symptoms of cerebral anoxia, such as fainting or vertigo.

Signs.—The asymmetry of the chest is evident. Cyanosis is not usually present, and clubbing is rare. The heart sounds may be normal or the pulmonary second sound may be accentuated or split. A sinus tachycardia is usually present.

Fluoroscopic and X-Ray Examination.—In the most common form of kyphoscoliosis, the thoracic curvature of the spine is to the right. As a result, the aorta is pulled to the right, and the heart is rotated clockwise around it long axis. The pulmonary artery becomes prominent, and the cardiac silhouette superficially resembles the configuration seen in mitral valvular disease (Fig. 106). However, on fluoroscopy, if the patient is turned slightly in the L.A.O. position, the cardiac shadow becomes normal, unless, of course, the kyphoscoliosis has resulted in right ventricular enlargement.

Kyphoscoliosis with the thoracic convexity to the left occurs less frequently. The aorta is pulled to the left, and the heart is rotated counterclockwise around its long axis, making the aortic knob prominent, and producing a superficial appearance of left ventricular enlargement. This can be corrected by fluoroscoping the patient in a slight R.A.O. position.

Electrocardiogram.—No significant findings are usually present. However, the patterns of chronic cor pulmonale (page 630) may appear.

Laboratory Tests.—Venous pressure and circulation time measurements give values similar to those found in chronic pulmonary disease (page 630).

Diagnosis.—Kyphoscoliosis should not be confused with a funnel chest (pectus excavatum) or a pigeon breast (pectus carinatum, see below).

Course and Prognosis.—Most patients with kyphoscoliosis die before the age of forty, either from heart failure or pulmonary infection. Sudden death is not uncommon.

Treatment.—There is no specific treatment for cor pulmonale resulting from kyphoscoliosis, although attempts should be made to correct the thoracic deformity in childhood. Morphine is contraindicated, because it may cause fatal respiratory depression.

Pectus Excavatum (Funnel chest).—In a funnel chest, the lower two-thirds of the sternum is depressed, compressing and displacing the heart *to the left. When the condition is mild, cardiac function is not affected* and cor pulmonale does not occur. However, when the depression

marked, there may be sufficient distortion and displacement of the heart and great vessels to produce an increased pulmonary resistance, pulmonary hypertension and cor pulmonale.

Symptoms may consist of dyspnea, precordial pain, palpitation. On *x*-ray examination, the displaced heart may resemble the silhouette of left ventricular enlargement, because the left ventricle appears rounded

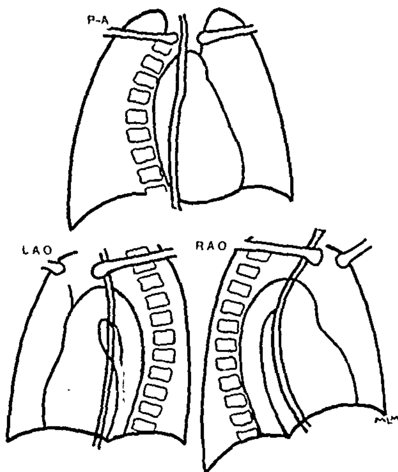


FIG 106 —Kyphoscoliosis.

However, a lateral *x*-ray view of the chest reveals the characteristic depressed sternum and decrease in the *P-A* diameter of the chest. Funnel chest can be corrected surgically if symptoms are severe.

Funnel chest should not be confused with a *pigeon breast* (*pectus carinatum*). Here, the thorax is compressed on either side of the sternum, which projects forward like a keel of a boat. A pigeon breast does not cause cardiac enlargement

Diffuse Interstitial Fibrosis of the Lungs.—This condition is characterized by an extreme degree of dyspnea and cyanosis which, in the course of a few weeks can cause cor pulmonale and death.

The etiology of interstitial fibrosis is unknown The acute phase occurs with an abrupt onset of cough, hemoptysis, dyspnea, cyanosis and fever If death occurs, the alveoli show necrosis of the alveolar and bronchiolar epithelium, marked edema and fibrosis in the alveolar walls, formation of a hyaline membrane which lines the alveoli, and an extensive, diffuse and progressive interstitial proliferation of fibrous tissue throughout all lobes of both lungs, associated with focal organization of intra-alveolar hemorrhages If the patient recovers, he develops a severe chronic cor pulmonale.

Chronic Cor Pulmonale Due to Embolism to the Pulmonary Artery or to Its Branches, or to the Pulmonary Arterioles.—If a patient with massive pulmonary embolism does not die, and if organization and recanalization of the embolus occurs, the affected pulmonary artery may offer such increased resistance to the flow of blood from the right ventricle that chronic cor pulmonale eventually results Similarly, multiple emboli to secondary pulmonary artery branches or even to the pulmonary arterioles, may also produce chronic cor pulmonale. At autopsy, in addition to the dilatation and hypertrophy of the right heart, the pulmonary arterioles in such cases often show a characteristic pathological picture which has been described as pulmonary endarteritis obliterans This consists of marked thickening of the intima with narrowing or even obliteration of the lumen of the vessel, and inflammatory changes throughout the vessel wall. However, similar changes may occur in the arterioles in cases of primary pulmonary arteriolar sclerosis. A similar clinical picture can occur from pulmonary arteriolar thrombosis occurring in patients with sickle cell anemia

The etiology of the cor pulmonale in such cases can be suspected from an initial history suggestive of massive pulmonary embolism, or a history of multiple attacks of "pneumonia." However, as in cases of pulmonary hypertension of unknown etiology, it may be very difficult to determine the etiology

The chronic cor pulmonale which may develop in patients with schistosomiasis is due to a similar occlusion of the smaller pulmonary arterioles, but here the vessels are occluded by schistosome ova which produce an inflammatory reaction in the vessels. In rare cases, chronic cor pulmonale may occur from partial occlusion of the pulmonary artery, not from a thrombus but from pressure on it by an aneurism of the aorta

Recent studies by Harrison in England have also raised doubt that primary pulmonary arteriosclerosis exists as a definite entity He injected broken fibrin clots into the pulmonary vascular system of rabbits and produced organized emboli. These lesions eventually became relined with a fibroelastic intimal thickening that was morphologically indistinguishable from spontaneous arteriosclerosis.

Cor Pulmonale Due to Carcinomatous Pulmonary Lymphangitis.—In cases of metastatic carcinoma to the lung, especially from a primary scirrhous carcinoma of the stomach (which may not even produce symptoms), the neoplastic cells may invade and obstruct the perivascular lymphatics to such an extent that they become as large as the arterioles. Compres-

sion and thrombosis of the arterioles follow, and there may even be carcinomatous invasion of the blood vessels.

The clinical course consists of cyanosis, cough, marked dyspnea, tachycardia and signs of progressive right-sided heart failure. Physical examination may reveal few abnormal signs, and there may not even be rales in the chest. However, on *x*-ray examination, the lymphangitic spread of the carcinoma produces a characteristic diffuse, string-like perivascular network with miliary nodules, radiating from the hilar regions. The electrocardiogram may show right ventricular strain (page 211).

The course is rapidly downhill with death due to right-sided failure in from two weeks to two months (unless the patient dies from the carcinoma in the meantime). For this reason the cardiac complications of carcinomatous pulmonary lymphangitis have been described as subacute cor pulmonale.

Ayerza's Disease and Syphilitic Pulmonary Arteritis.—In 1901, Abel Ayerza of Argentina, described in an unpublished clinical lecture a case of heart failure with such marked cyanosis that the patient was almost black (cardiaco negro). At autopsy, there were dilatation of the bronchi, peribronchitis and hypertrophy and dilatation of the right auricle and right ventricle. The pulmonary arteries were not described. Some years later, this clinical picture was called Ayerza's disease, and was considered to be due to syphilitic pulmonary arteritis. However, although syphilis can affect the pulmonary artery and its major branches, and may even produce a pulmonary artery aneurism, such lesions are incapable of producing the clinical picture that Ayerza described. More recently, the term Ayerza's disease, or Ayerza's syndrome has been used merely to describe cases of chronic cor pulmonale with intense cyanosis and right-sided heart failure, regardless of the etiology of the cor pulmonale.

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Chapter 41

DISEASES OF THE PERICARDIUM

Classification.—The pericardium may be affected by acute or chronic inflammation, by trauma, by malignant tumors, and in many other ways. The various conditions causing pericardial disease can be classified in the following way:

ACUTE PERICARDITIS

Pathology.—The physical picture of pericarditis may vary greatly. In *fibrinous pericarditis, an exudate of fibrin*, white blood cells and some endothelial cells usually covers the parietal and visceral layers of the pericardium. When thick, it has a stringy, shaggy, irregular, "bread and butter" appearance. The exudate may be localized to one region of the heart

or may be generalized. There is usually some exudation of fluid even in a fibrinous pericarditis, but in a serofibrinous pericarditis, a serous exudate appears in varying amounts from 100 cc. to 2 or 3 liters (Normally, the pericardium contains less than 35 or 50 cc. of fluid.) The exudate may be either straw-colored, or turbid due to the presence of white blood cells and desquamated endothelial cells. Occasionally numerous red blood cells in the exudate give it a hemorrhagic appearance This should not be confused with a hemopericardium (page 654) In cases of pericarditis due to pyogenic organisms, the exudate may become frankly purulent and thick. In such cases, the volume of fluid is usually less than 250 cc., but may be much more In both fibrinous and serofibrinous pericarditis, inflammatory changes in the subepicardial myocardium are usually present.

With healing, the fluid may be resorbed in two or three weeks or even in a shorter period of time, and all signs of the inflammation may disappear. However, in a condition, such as tuberculous pericarditis, the effusion may last for months or longer

Milk spots, which are small, whitish, flat plaques on the visceral layer of the pericardium especially over the right ventricle where it is not covered by the lung, may be signs of a healed pericarditis However, they may be merely produced mechanically by the heart rubbing against the chest wall during systole In other cases, various degrees of adhesions between the parietal and visceral pericardial layers may occur, and in some cases the pericardial cavity may be completely obliterated (see Chronic Constrictive Pericarditis, page 650). Adhesions may even extend to the mediastinal structures. Rarely, pericardial adhesions cause a sacculated effusion to form

Pathological Physiology.—Fibrinous pericarditis and even a moderate pericardial effusion may not alter cardiovascular dynamics to any extent. However, a large effusion, or even a small effusion of 250 to 350 cc. which accumulates rapidly, interferes with the diastolic filling of the heart and produces the clinical picture of cardiac tamponade (acute compression of the heart) in the following way. when a pericardial effusion forms slowly, the pericardium can stretch greatly to accommodate the increased volume of fluid without producing a rise in intrapericardial pressure. However, if the effusion forms rapidly, the pericardial sac cannot stretch rapidly enough, and the intrapericardial pressure rises greatly. A rise in intrapericardial pressure occurs even with a slowly formed effusion, if it is large enough. The increased intrapericardial pressure prevents the heart from expanding adequately in diastole, less blood enters the heart, and the stroke volume and cardiac output fall As a compensatory mechanism, the heart rate increases

Because of the increased intrapericardial pressure, venous blood is unable to return to the right heart, and the right auricular pressure and the venous pressure rise. In addition the arm-to-tongue circulation time is prolonged because of the slowing of the circulation. The rise in venous pressure occurs not only because of the increased intrapericardial pressure but also as a compensatory mechanism, possibly by means of neurogenic reflexes, to enable more blood to be returned to the right heart. For this reason, venous infusions, which further increase the venous pressure, have been used to

restore the cardiac output toward normal temporarily in cases of pericardial tamponade, until the tamponade can be relieved.

Symptoms.—The symptoms of pericarditis can be described as follows:

1. **General Symptoms Which Depend on the Etiology of the Pericarditis.**—In many conditions, such as acute rheumatic fever, uremia, myocardial infarction, malignancy, *etc.*, the pericarditis is almost a minor complication of a primary, serious disease, and may be completely overlooked clinically, to be diagnosed only at the autopsy table. Fever may or may not be present. In cases of purulent pericarditis due to pyogenic organisms, a septic temperature may be present with great prostration.

2. **Precordial Pain.**—Precordial pain may or may not be present, because the visceral pericardium is completely insensitive to pain, and only a portion of the parietal pericardium, especially its anterior surface at a low level, is sensitive. The pain may be sharp, or dull and pressing, and may be referred to the epigastrium, left shoulder, neck, and left arm. It is often increased by inspiration, cough or movement of the chest. The pain may be so severe as to simulate an attack of acute myocardial infarction. The patient usually feels more comfortable sitting than lying.

3. **Symptoms Due to Pericardial Effusion.**—A dry cough may occur, due to compression of the bronchi or lungs by the effusion, which also decreases the vital capacity and produces an increased respiratory rate and *dyspnea*. (The vital capacity may also be decreased because of pulmonary stasis due to compression of the pulmonary veins by the pericardial effusion.) Pressure of the distended pericardium on the esophagus may cause dysphagia.

Signs.—The signs of pericarditis are due to (1) rubbing together of the inflamed pericardial surfaces, producing a pericardial friction rub; (2) the *presence or absence of pericardial effusion, and (3) signs of associated disease processes.*

1. **Pericardial Friction Rub.**—A pericardial friction rub (page 160) occurs characteristically with a dry, fibrinous pericarditis, but it also may be present even if there is a large effusion. The friction rub is often inconstant and may last only for a few hours. In other cases, it may persist for weeks or longer.

2. **Physical Signs of Pericardial Effusion.**—These signs are dependent on the volume of fluid in the pericardium and the rapidity with which it has accumulated. The nature of the fluid, whether it is an exudate, transudate, or an accumulation of blood, *etc.*, is unimportant.

The patient is often restless and uncomfortable and often is found sitting in bed, with his trunk bent forward. This tends to draw the fluid anteriorly and away from the lungs. Occasionally, the patient finds that he gets *relief* by assuming a knee-chest position. He is often pale due to peripheral vasoconstriction (or to anemia due to rheumatic fever, uremia or the condition responsible for the pericarditis), but may show facial cyanosis and even slight facial edema due to the increased venous pressure and venous stasis, which also causes the neck veins to be greatly distended.

The blood pressure tends to be *low*, with a small *pulse pressure*, due to the decreased cardiac output. With acute pericardial tamponade, the clinical picture of shock (page 283) associated with venous engorgement may occur. A paradoxical pulse (page 141) is usually present, with or without inspiratory swelling of the neck veins (page 148).

The Heart.—The area of relative cardiac dullness enlarges greatly, and even extends up to the first intercostal space The area of total cardiac flatness is characteristically almost as large as the area of cardiac dullness (page 157, and Fig 39, *B*, page 156), producing an abrupt transition from flatness to resonance In addition, there is widening of the area of dullness on percussion in the first and second intercostal spaces, especially on lying This area becomes narrower when the patient sits and the fluid shifts because of gravity. The acute cardiohepatic angle disappears and becomes obtuse (Rotch's sign, page 157), and dullness and bronchial breath sounds may appear below the angle of the left scapula (Ewart's sign, page 171). The heart sounds may or may not be distant, and the apical impulse may not only remain palpable but also visible. However, the apical impulse is found well within the left border of cardiac dullness

Engorgement and enlargement of the liver may occur in the following way the distended pericardium presses on the dome of the diaphragm and the diaphragmatic surface of the liver, thus compressing the hepatic veins which open into the inferior vena cava just below the diaphragm The left hepatic vein is particularly affected since it runs almost parallel to the diaphragmatic surface of the liver during its terminal course. The engorgement of the liver also produces portal vein hypertension and ascites may also appear Part of the hepatic engorgement is also due to the increased pressure in the inferior vena cava, which may also result in edema of the lower extremities.

Fluoroscopic and X-Ray Signs of Pericardial Effusion.—These have already been described on page 196 An effusion of less than 250 cc. in adults and 150 cc. in children probably cannot be recognized by x-ray or even by physical examination

Occasionally a sacculated pericardial effusion occurs This is usually of rheumatic origin It usually appears on the right side of the heart, and may resemble an aneurism of the sinus of Valsalva, a pericardial diverticulum, a tumor of the pericardium or a pleural, pulmonary or mediastinal tumor

Angiocardiographic Examination.—A characteristic shadow due to the pericardial effusion appears outside of and surrounds the opacified chambers of the heart

Electrocardiogram—The electrocardiogram may remain normal in spite of pericarditis or pericardial effusion. Pericarditis produces electrocardiographic changes because of the presence of superficial injury to the epicardial surface of the heart, and abnormal *RS–T* deviations may appear, with *T* wave changes later developing, similar to the changes which occur after myocardial infarction.

RS–T elevations may appear in one or more of the precordial leads, especially from the left side of the chest, in leads *aVL*, *aVF*, and in leads I, II, and even lead III Lead *aVR* shows an abnormal depression of the *RS–T*. These *RS–T* deviations usually last for only a day or two and then return to the base line Symmetrical *T* waves then develop and last as long as the pericarditis and the myocardial injury persist. The *T* waves do not become as deep and tall as those seen after myocardial infarction (see also page 601). Abnormal *Q* waves, however, do not develop because the myocardial injury is superficial (page 201)

When pericardial effusion is present, the fluid may short-circuit the electrical currents spreading from the heart so that low voltage of the *QRS* complexes may appear in the standard and augmented unipolar extremity leads.

Diagnosis.—Although the only physical sign of a fibrinous pericarditis is a friction rub, the electrocardiogram may show characteristic *RS-T* deviations even in the absence of physical findings. A pericardial effusion on the other hand should be suspected when a patient shows dyspnea and tachycardia with enlargement of the heart, distended neck veins and a large liver, and the usual causes of heart failure are absent.

A pericardial effusion can be simulated by the generalized cardiac dilatation due to heart failure, and the differential diagnosis between these two conditions may be very difficult and may require a diagnostic tap (see page 648). However, failure to withdraw fluid with the needle does not prove that fluid is absent, because the fluid may be encapsulated. However, if a pulsus paradoxicus and inspiratory filling of the neck veins are present, this is almost pathognomonic of either a massive pericardial effusion or constrictive pericarditis.

The differentiation of pericarditis from acute myocardial infarction is described on page 600.

The etiology of a pericardial effusion can sometimes be determined by pericardial tap. A pericardial exudate shows a protein content above 3 per cent, and a specific gravity above 1.018 in contradistinction to a pericardial transudate, such as occurs in congestive heart failure, or in the anasarca of nephritis or hypoproteinemia. Hemorrhagic pericardial fluid is common in tuberculosis and malignancy, but may occur in severe rheumatic fever, after trauma, *etc.* Uremia and myocardial infarction are usually associated with a fibrinous pericarditis rather than with pericarditis with effusion. In tuberculous pericarditis, and in malignancy, massive effusions are common and tend to reaccumulate.

The exudate is usually sterile, but if purulent, contains organisms. It may be necessary to do a guinea pig inoculation to determine a tuberculous etiology. Study of a centrifuged sediment may reveal malignant cells, and may even reveal tubercle bacilli.

Course and Prognosis.—The course and prognosis of pericarditis depends on the etiology. Some of the more common forms of pericarditis can be discussed briefly as follows.

Acute Nonspecific (Benign) Pericarditis.—Acute *nonspecific pericarditis* usually affects young adults. It occurs a week or so after the onset of an upper respiratory or grippe-like infection. The onset may be very sudden with severe crushing substernal pain and even a shock-like picture. A rapid rise in temperature, even to 104° or higher occurs during the first day, then it begins to fall. The white blood count and sedimentation rate are also increased even on the first day, and *return to normal in a week or two.*

Examination of the heart usually reveals a rough friction rub and physical and *x*-ray signs of marked cardiac enlargement, even the first day. However, much of the enlargement of the heart shadow which appears on *x*-ray examination is probably due to acute dilatation of the heart, because pericardial tap is often unsuccessful, and because the patient does not show

signs of pericardial tamponade in spite of the markedly enlarged heart The electrocardiogram shows the typical patterns of pericarditis. The *T* wave changes may persist for several weeks

Examination of the lungs often reveals a unilateral or bilateral pleural effusion.

The temperature usually returns to normal within a week. However, a low-grade fever may continue for two or three weeks The precordial pain usually disappears in two or three days, but an annoying and nagging precordial pain may persist for several months, and the patient may develop symptoms of neurocirculatory asthenia or of a cardiac neurosis However, one or more recurrences of the pericarditis may occur. It is also possible that some cases of chronic constrictive pericarditis may occur as a result of acute nonspecific pericarditis

Acute Bacterial (Purulent) Pericarditis —Pneumococci, group A hemolytic streptococci, and staphylococci are usually the causative organisms, but the meningococcus, gonococcus, P. tularensis, and even gas-forming organisms can invade the pericardium Invasion can take place by direct extension from a pulmonary, pleural or mediastinal infection, during the course of a septicemia, as a result of penetrating wounds of the pericardium, and rarely, from extension of a subdiaphragmatic abscess

In the past, the condition was invariably fatal unless the pericardium was surgically drained by resecting part of the ribs or sternum However, use of the newer antibiotics has considerably reduced both the incidence and mortality of purulent pericarditis, and has even obviated surgical drainage in many cases

Rheumatic Pericarditis —This is common, especially in children, during the course of acute rheumatic fever. It occurs in association with a pancarditis, and the child may die There may or may not be a large effusion Under salicylate therapy, mercurials and oxygen, even large exudates can be reabsorbed in two or three weeks It is rarely necessary to tap the pericardium Although pericardial adhesions may form, chronic constrictive pericarditis does not occur after rheumatic pericarditis

Tuberculous Pericarditis —Tuberculous pericarditis usually occurs from extension of a pulmonary, hilar or mediastinal gland lesion A chronic serofibrinous pericarditis occurs with tubercles and caseation Hemorrhagic effusion is common and massive effusion, even 2 or 3 liters may occur A fistulous tract to the skin may form

The clinical course is insidious and usually downward, and death may occur in three to six months However, the patient may recover and develop chronic constrictive pericarditis

Treatment.—Tuberculous pericarditis should be treated vigorously with intermittent streptomycin and daily para-aminosalicylic acid or isoniazid Two grams of streptomycin can be given every third day In addition, 12 grams of para-aminosalicylic acid, or 300 mg. of isoniazid are given daily Treatment should be continued for a minimum of four months. The optimum length of treatment is probably eight to twelve months

The actual duration of treatment will depend on the response of the patient However, it should be continued for three to six months after all signs of activity have disappeared

The following criteria can be used to indicate that the tuberculous process has become inactive: 1, the patient is afebrile, 2, the sedimentation rate has become normal; 3, the heart shows a normal size and has normal pulsations; 4, the electrocardiogram is stable, even though it is not normal After chemotherapy is stopped, the patient is slowly ambulated.

If the patient shows persistent or progressive congestion in spite of the above treatment, surgery should be done even though active disease is present.

Uremic Pericarditis.—Uremic pericarditis usually occurs in the terminal stages of renal disease. Death usually occurs in a few days to several weeks, but the patient may sometimes live several months if renal function improves It is usually a fibrinous pericarditis, but effusion may occur. Uremic pericarditis is possibly produced by chemical and metabolic alterations in the body resulting from the uremia.

Pericarditis Secondary to Myocardial Infarction—There is often a patch of pericarditis over the epicardial surface of the infarct, but occasionally a generalized serofibrinous pericarditis occurs, sometimes with marked effusion. It does not alter the course of the infarct

Treatment.—The treatment of pericarditis is that of the underlying disease. However, a purulent pericarditis may require surgical drainage in addition to antibiotic therapy. Penicillin can even be instilled into the pericardium in the following way: after aspiration of the exudate, the pericardial cavity can be irrigated with sterile, isotonic, saline solution if necessary Then from 50,000 to 200,000 units of penicillin is reinjected in a volume of solution less than the volume of pus aspirated

Aspiration of pericardial fluid is necessary only in cases of pericardial tamponade, in cases of purulent pericarditis, and for diagnostic purposes As much as 1000 cc. of fluid can be safely removed at one time, although the patient often feels improved even when only a few hundred cc. are removed In cases of tuberculous pericarditis, it has been customary after the fluid has been withdrawn, to replace half as much air

Technic of Pericardial Paracentesis.—The needle can be inserted in the following sites:

1 *The Apical Approach*, in the fifth left intercostal space, 1 or 2 cm within the left outer border of cardiac dullness. This is the most commonly used site.

Technic.—The patient is supported in a sitting position in bed, and the left border of cardiac dullness and left diaphragm are outlined by percussion. Fluoroscopy may be necessary to check these landmarks. The fifth left interspace is then identified

The skin of the area is prepared with an antiseptic solution The skin and subcutaneous tissues are then infiltrated with a 2 per cent procaine solution, using aseptic precautions. A short-beveled 18 gage needle, attached to a 5 to 10 cc syringe for ease of manipulation is then inserted in the fifth left interspace within the left outer border of cardiac dullness, but beyond the apical impulse, if this can be felt. The needle is directed posteriorly and medially toward the spine, while suction is maintained with the plunger.

The depth of penetration will vary. It usually does not exceed [illegible] cm. If a grating sensation is felt, or if a pulsation synchronous with the heart beat is imparted to the needle, the needle should be withdrawn slightly. If fluid is not obtained with two or three advances of the needle, the attempt should be abandoned. When fluid is obtained, the needle should be connected to a 50 cc. syringe by means of a soft rubber tube and a 3-way stop-cock in order to complete the aspiration without further movement of the needle. It may be necessary to use a trocar, or even to employ surgical drainage to aspirate a thick purulent exudate.

2. *The Subxiphoid Approach.*—This can be used as an alternate method of pericardial paracentesis.

Technic.—The patient is placed in a reclining position with pillows under the back to cause the xiphoid process to protrude anteriorly. The skin over the xiphoid area is antiseptically prepared and anesthetized with a [illegible] per cent procaine solution.

A lumbar puncture needle without stylet (17 or 18 gauge and [illegible] to [illegible] cm. long) is inserted just below and close to the xiphoid process in the midline. The tip of the needle is directed upward and kept in contact with the posterior side of the xiphoid and the sternum. As the needle is slowly and carefully inserted, the adapter end of the needle is pressed down against the skin of the abdomen. In this way, the needle runs along the posterior surface of the sternum until it enters the pericardial cavity. In children under five years of age, the tip of the needle must penetrate to a depth of about [illegible] cm. in order to reach the pericardial cavity. In adults, it must penetrate about 6 or 7 cm. If fluid is not readily obtained, the procedure may be varied by directing the bevel of the needle 45° posteriorly and pointing it toward the left shoulder.

3. The needle can also be inserted in the fourth intercostal space to the right (or left) of the sternum. The point to the right of the sternum is especially good for aspirating local encapsulated effusions on the right side.

Pericardial paracentesis may be dangerous. The cavity of the heart may be penetrated. This can be suspected if pure blood is aspirated and there is no history of trauma. A coronary artery can be lacerated and hemopericardium may result. The patient may develop shock or ventricular tachycardia. Death may occur following the paracentesis.

CHRONIC ADHESIVE PERICARDITIS

In chronic adhesive pericarditis, very marked adhesions form between the parietal and visceral layers of the pericardium (concretio cordis) or between the parietal pericardium and the mediastinum, sternum, ribs or the diaphragm (mediastinopericarditis). Such adhesions do not disturb the function of the heart, although in the past, some cardiologists believed that the pericardial adhesions, especially to the chest wall, were the cause of marked cardiac hypertrophy and dilatation. However, in all such cases the valvular lesions which are present are sufficient to have produced the enlargement of the heart. Furthermore, it has been shown that when intra- and extra-pericardial adhesions are produced experimentally, such adhesions do not produce cardiac enlargement.

Adhesive pericarditis itself does not produce symptoms, and most of the physical signs which have been described for adhesive pericarditis are due to concomitant chronic valvular disease or to chronic constrictive pericarditis which may be present.

A common cause of adhesive pericarditis is rheumatic fever, which probably never causes chronic constrictive pericarditis.

CHRONIC CONSTRICTIVE PERICARDITIS

In chronic constrictive pericarditis (concretio cordis), the heart is encased in a thick, dense, fibrous pericardial shell which prevents the heart from expanding adequately in diastole.

Pathological Physiology.—As a result of chronic pericardial inflammation, the parietal and visceral layers of the pericardium become inelastic and from 3 mm. to 1 cm thick. In addition, the pericardial cavity may be completely obliterated as a result of adhesions between the two layers. The thickened pericardium may extend over the entire heart or may be localized to the ventricles Local or generalized calcification of the parietal or visceral layers or both may occur. Adhesions between the parietal pericardium and the diaphragm or ribs or sternum may or may not be present

The thickened pericardium interferes with the normal diastolic expansion of the heart. As a result, less blood is able to enter the heart during diastole, the cardiac output falls and remains below normal Therefore, the heart does not dilate or hypertrophy and may actually atrophy However, the heart may be enlarged in cases of chronic constrictive pericarditis. In such cases, the enlargement occurred before the chronic constrictive pericarditis developed. Valvular lesions are absent. If present, they are due to antecedent valvular disease

Because of the decreased cardiac output, blood accumulates within the venous system, and a marked rise in venous pressure occurs, along with a rise in circulating blood volume, producing the clinical picture of chronic cardiac tamponade (page 643) Constriction of the pulmonary veins by the fibrosed pericardium may also produce pulmonary stasis and an increased pulmonary pressure which is transmitted to the right ventricle and the right auricle This may also result in pleural effusion. Constriction of the auriculoventricular grooves by fibrosed bands may cause marked dilatation of the auricles.

The liver is greatly engorged and covered with a thick exudate This is not inflammatory in origin but is associated with the very marked increase in venous pressure within the liver Microscopically, the typical changes of chronic right-sided heart failure appear (page 243), although in the past these changes have been described as *pseudocirrhosis of the liver*. Congestion of other abdominal organs, such as the kidneys, and spleen, also occurs, as well as ascites.

The enlargement of the liver and the ascites are due in part to the increased pressure in the hepatic veins transmitted from the inferior vena cava This in turn results in portal hypertension (also see page 645). However, another explanation is that the extension of the pericarditis to the diaphragm causes obliteration of the lymphatics from the liver and perito-

neum which penetrate the diaphragm to reach the thorax. Similarly, adhesions around the inferior vena cava compress the lymphatic vessels from the liver and abdominal cavity which run alongside the inferior vena cava

In spite of the very high pressure in the inferior vena cava, edema of the lower extremities may not be marked, and is usually less prominent than the ascites (The lack of relation between a high venous pressure and the development of edema is discussed on page 128.)

Hypoproteinemia, due to a reduction in serum albumin, the globulin remaining normal or becoming elevated, is a common finding This may be due to impaired liver function, or possibly to the loss of albumin contained in the ascitic fluid, if repeated taps are done

Etiology.—The most common cause of chronic constrictive pericarditis is a tuberculous pericarditis It does not occur as a result of rheumatic pericarditis. In many cases the etiology is unknown and the onset insidious, and there may not even be a history of a previous attack of acute pericarditis Rarely, the clinical picture of chronic constrictive pericarditis can be produced by a foreign body in the pericardium, or by a tumor of the heart or pericardium, or as a result of strangulation of the heart through a tear in the pericardium

Symptoms.—The low cardiac output, the high venous pressure and the pulmonary and venous engorgement may produce weakness and dyspnea on exertion, but these symptoms are often mild or may be absent, and the patient's chief complaint is often abdominal distention due to the marked ascites The dyspnea is exertional in type, and the patient is often able to lie flat in bed at rest

Syncopal attacks may occur during exertion This is due to the fact that the cardiac output cannot increase and meet the demands required by exertion

Signs.—Mild cyanosis is common. This is a peripheral cyanosis and is due to stagnation

The vital capacity is low. This may be due to pulmonary congestion or to the fact that ascites is present and elevates the domes of the diaphragm

The blood pressure is often low with a small pulse pressure, and a pulsus paradoxicus (page 141) is usually present, unless pulmonary stagnation is marked The neck veins are distended and do not appear to pulsate, but inspiratory swelling of the neck veins may occur (page 148) In the lungs, rales and signs of pleural effusion may be present Massive ascites may mask the enlargement of the liver A characteristic feature of the ascites is its tendency to reaccumulate after abdominal paracentesis Edema of the lower extremities may be minimal, as was mentioned above

A friction rub over the liver, synchronous with respiration can sometimes be felt and heard

The heart does not appear to be enlarged on physical examination The heart sounds may be distant Murmurs are usually absent, or if present, are not related to the constrictive pericarditis An apical systolic murmur may be present, the cause of which is not clear. Sinus rhythm is usually present, with a sinus tachycardia, but auricular fibrillation is common

An adventitious diastolic sound is often present This simulates a third heart sound. The cause of this extra heart sound is not known. However,

it only appears in cases with calcification of the pericardium In rare cases, rheumatic heart disease is present, as a coincidental finding

Fluoroscopic and X-Ray Examination.—The following findings are common. The heart is usually small and normal in size but may be moderately or even markedly enlarged It may show an abnormal triangular or globular shape due to the loss of the normal subdivisions of the chambers The aortic arch is small and flattened or may be absent. The hilar markings are increased and there is evidence of pulmonary congestion

On fluoroscopy the following signs are present:

1. There is a decrease in the amplitude of cardiac pulsations This can be confirmed with roentgenkymographic or electrokymographic examination However, the amplitude of cardiac pulsations may be increased due to a change in the manner of contraction (The longitudinal contraction of the ventricular wall is interfered with by the adhesions, and this reduction of movement is compensated for by increased marginal contractions. These increased pulsations are most often observed over the left lower border where the fibrosed pericardium is usually thinnest.)

Electrokymographic examination reveals a characteristic if not pathognomonic finding, namely, that while the ascending limb of the rapid diastolic filling phase of the electrokymogram begins normally, it ends abruptly in a sustained plateau after completing a portion of the upstroke, and remains on a plateau until the injection phase of systole begins Apparently the constrictive pericarditis stops outward motion of the ventricular wall shortly after the ventricles begin to fill

2 The heart does not elongate as the diaphragm descends on inspiration This sign is valuable only if the heart is not greatly enlarged, and if the diaphragm is able to descend normally The presence of marked ascites would prevent this

3 The heart does not shift if the patient bends from side to side.

4 Paradoxical motion of, or deformity of the diaphragm appears, due to tugging of pericardial adhesions When the patient takes a deep breath, the diaphragm is observed to rise during systole

5 The superior vena cava is greatly dilated (see page 192)

X-Ray Signs of Calcification of the Pericardium.—This is a reliable confirmatory sign of chronic constrictive pericarditis, but it is present in less than half the cases, and when present, does not necessarily indicate that constriction is present It is often best demonstrated in an oblique or lateral position, using heavy exposures. The calcification may be observed as streaks, bands or plaques, which may even form a shell around the heart. The calcification is predominant on, and sometimes limited to the diaphragmatic surface of the heart. This may be due to sedimentation of inflammatory particles which later become calcified The calcification also tends to be dense in the atrio-ventricular groove The apex is usually free of calcification.

Calcification of the pericardium should not be confused with calcification of a coronary artery or of the heart valves (see page 196).

Electrocardiogram.—The secondary *T* wave changes of pericarditis are usually present (page 645). There may or may not be low voltage of the *QRS* complex (page 201).

Catheterization Studies.—Catheterization of the right ventricle shows a very characteristic pattern, namely, an early diastolic dip followed by a diastolic plateau If this is associated with an end-diastolic right ventricular pressure which is more than one-third the pressure in the right ventricle during systole, a diagnosis of constrictive pericarditis can be definitely made

Laboratory Tests.—The venous pressure varies from 20 to 40 cm of water, and rises markedly even after mild exercise, such as squeezing a rubber bulb in the hand This observation has been used to differentiate the increased venous pressure of pericarditis (or superior vena caval obstruction) from that due to chronic right-sided heart failure, because in right-sided heart failure there is no obstruction to the return of venous blood to the heart, and no marked rise in venous pressure occurs after mild exercise.

The arm-to-tongue circulation time is prolonged Arm-to-lung circulation time also is prolonged, but may be normal The reason for a normal arm-to-lung time in the presence of a high venous pressure is not known

Serum albumin values are often very low This is due to the inability of the engorged liver to manufacture protein. Another cause is a loss of serum albumin from repeated abdominal paracenteses

Diagnosis.—The most common signs of chronic constrictive pericarditis are a paradoxical pulse, ascites, distention of the neck veins and mild cyanosis associated with a small heart. *X*-ray signs of pericardial calcification or *T* wave abnormalities in the electrocardiogram serve to confirm the diagnosis

Chronic constrictive pericarditis can be simulated by cirrhosis of the liver because of the early development of ascites However, in cirrhosis, the neck veins are not distended, the venous pressure of the upper extremities is normal, and a paradoxical pulse is not present.

Chronic right-sided heart failure may also simulate chronic constrictive pericarditis, but here the heart is usually very large, and characteristic signs of valvular disease are usually present

Course and Prognosis.—Patients who do not receive surgical treatment run a slow but progressively downhill course, but may live for many years in semi-invalidism Death may result from intestinal perforation and peritonitis complicating an abdominal paracentesis, or from intercurrent infection

Treatment.—There is only one effective treatment, namely, surgical decortication of the heart (partial pericardiectomy) It is not necessary and often not possible to remove the thickened pericardium from the entire surface of the heart. The first area to be freed is the anterior surface of the left ventricle so that it can receive the increased blood that flows into it after decortication of the right ventricle Constricting bands around the pulmonary veins or inferior or superior vena cava should always be cut During the decortication there is always the danger that a coronary artery will be severed or the underlying myocardium injured, and ventricular fibrillation may occur as a result of excess cardiac manipulation To avoid this, a few cc. of 5 per cent procaine solution can be applied to the surfaces of the heart which appear irritable. Even if ventricular fibrillation does

occur, it can be stopped (see page 763). The use of intravenous procaine during the operation may also forestall the development of ventricular fibrillation

The success of decortication can be seen during the operation because the heart enlarges and bulges through the opening in the pericardium and beats more forcibly However, in spite of a successful operation it may take even six months for the complete disappearance of signs and symptoms, and if sufficient pericardium has not been removed, complete recovery may not take place

Active tuberculous pericarditis is a contraindication to operation, but decortication may be necessary even in the presence of activity if the patient shows signs of progressive cardiac tamponade. The operative mortality is about 15 per cent

NON-INFLAMMATORY PERICARDIAL EFFUSIONS

Hydropericardium.—Hydropericardium consists of an accumulation of non-inflammatory transudate which is clear, has a specific gravity of less than 1.018, and a protein content less than 3 per cent It occurs as part of anasarca due to congestive heart failure, or nephritis, in cases of of beriberi, or with hypoproteinemia. The pericardial effusion of myxedema is usually described as a transudate but its specific gravity and protein content may be high Hydropericardium may even occur as a result of mediastinal tumors which interfere with the venous or lymphatic drainage of the pericardium.

Hemopericardium.—Hemopericardium consists of an accumulation of gross blood in the pericardium. It may occur in several ways:

1 Rupture of the heart. Death usually occurs instantly or within half an hour Rupture of the left, sometimes the right ventricle, or even the auricles may occur after myocardial infarction, especially within the first two weeks Rarely, an abscess, tumor or cyst of the muscle wall ruptures

Hemopericardium may also occur after myocardial infarction in the absence of rupture of the heart It can also be produced by excessive anticoagulant therapy

2 Rupture of the first portion of the ascending aorta. This may be due to severe trauma to the chest, to a syphilitic or mycotic aneurism, an aneurism of the sinus of Valsalva, or a dissecting aneurism of the aorta.

3 Rupture of a coronary artery (see page 519).

4 Miscellaneous conditions such as tuberculosis, neoplasm, hemorrhagic diseases, infections, and chronic nephritis

Pneumopericardium.—Pneumopericardium consists of air in the pericardium There may also be fluid (hydropneumopericardium) or pus (pyopneumopericardium) It can occur in association with pulmonary tuberculosis, from trauma to the chest; from perforation of the esophagus or other air-containing organs; as a result of pericarditis due to a gas-forming organism, or simply as a result of introducing air during a pericardial tap.

Pneumopericardium itself usually produces no symptoms, but may cause pericardial tamponade if enough air is trapped. A large volume of air may result in tympany on percussion, and clinking sounds may be heard on

auscultation If a hydropneumopericardium is present, gurgling and splashing sounds may be heard with each heart beat

On x-ray examination, the air separating the pericardium from the heart causes the pericardial shadow to be seen as a faint, curved line surrounding the heart. A horizontal fluid level within the pericardium is seen in hydropneumopericardium.

It is not necessary to remove the air unless signs of tamponade are present.

Chylopericardium.—This is a rare condition in which milky lymph from the thoracic duct enters the pericardium as a result of trauma or a malignant tumor.

PERICARDIAL DIVERTICULA

Pericardial diverticula or cysts may be acquired or congenital. They are usually symptomless, but may cause substernal pressure, and can bulge into the anterior chest wall.

On x-ray examination, the diverticulum is seen as an oval mass protruding from the cardiac shadow, most commonly on the right lower border of the heart. A similar x-ray picture can be produced by an encapsulated pericardial effusion

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Chapter 42

DISEASES OF THE AORTA, PULMONARY ARTERY, AND OTHER BLOOD VESSELS

DISEASES OF THE AORTA

THE more important diseases affecting the aorta are:

1 *Atherosclerosis of the Aorta* (page 581)

2 *Aortitis.*—This is usually syphilitic (page 543), but may occur with rheumatic fever, bacterial endocarditis and other infections

3 *Aneurisms of the Aorta* (page 546) —These are usually syphilitic, but may be mycotic, traumatic, congenital or of unknown etiology.

4 *Congenital Malformations of the Aorta* —These include coarctation of the aorta (page 453), hypoplasia or absence of the aortic arch (page 460), right or double aortic arch (page 441), congenital aneurism of the right sinus of Valsalva (page 429), transposition of the aorta and pulmonary artery (page 447), defect of the aortic wall (page 470), and patent ductus arteriosus (page 464)

5 *Dynamic Dilatation of the Aorta* (page 536)

6 *Dissecting Aneurism of the Aorta*

DISSECTING ANEURISM OF THE AORTA

The basic pathology of dissecting aneurism of the aorta is a cystic necrosis of the media which shows marked loss of both smooth muscle and elastic tissues and the presence of mucoid-filled cysts and "faults," (*medionecrosis aortae idiopathica cystica*)

Pathology.—The dissection of the aortic wall probably starts as a small hemorrhage in the media, due to rupture of one of the vasa vasorum. This in turn causes a transverse or oblique tear in the intima which allows large quantities of blood to be forced into the diseased aortic wall through the intimal tear, splitting the media for a variable distance up or down. The tear in the intima occurs mainly in two locations: in the ascending aorta just above the aortic valve, which is where the aorta is subject to its greatest strain, and at the isthmus of the aorta near the location of the ligamentum arteriosum However, the dissection may start at any point in the aorta Rarely, the intimal tear occurs in an atherosclerotic plaque

The length of the dissecting column is variable and in some cases may extend from the aortic valve to the termination of the aorta at the bifurcation of the common iliac arteries Frequently, rupture of the aorta may occur with massive hemorrhage into the pericardium, or into the right or left pleural cavity, into the mediastinum, or retroperitoneally or into the abdomen Occasionally, the dissecting column of blood may rupture into the lumen of the aorta at some point from the original intimal tear, producing

a so-called double-barrelled aorta, which may later become lined with endothelium if the patient survives.

As the dissecting column of blood spreads through the aorta it may compress and occlude the branches of the aorta, such as the innominate, carotid, left subclavian, intercostal, renal, mesenteric, lumbar, even the coronary arteries.

Etiology.—The etiology of the cystic necrosis of the aortic media, or of the dissecting aneurism is unknown. Most patients with a dissecting aneurism have hypertension It is frequent in males, especially above the age of forty years, but it also occurs in the younger age groups, and in women, especially during pregnancy. It also occurs in cases of coarctation of the aorta, and with arachnodactyly There is often a history of unusual effort or excitement just prior to the attack

Symptoms.—The symptoms are due to the pain resulting from the splitting of the aortic wall, and from the disturbances in blood supply produced by compression and occlusion of the aortic branches.

The pain is intense. It may be burning, constricting or tearing It usually begins anteriorly over the precordium, but may radiate to the arms, the neck, jaws, and head, to the back, the abdomen and finally into the legs Nausea and vomiting may occur as well as hoarseness or dysphagia, due to pressure from the widened aorta When the carotid arteries are involved, fainting, coma, transient loss of vision or hemiplegia may occur as a result of cerebral ischemia Involvement of the intercostal or lumbar arteries may cause ischemia of the spine with numbness or paresthesias of the extremities, weakness of the lower extremities and even paraplegia Intense abdominal pain may occur if the renal, mesenteric or other arteries supplying the abdominal viscera are compressed or occluded

Signs.—*Although the patient may present the cold,* clammy appearance of shock, the blood pressure may remain comparatively high, or even if it falls, it often rises again even to markedly hypertensive levels in from twenty-four to forty-eight hours Obliteration of the innominate or left subclavian artery may cause bilateral inequality of the pulse and blood pressure There may also be inequality of the carotid or radial pulses with weak femoral pulses A unilateral reduplication of the carotid pulse has also been described as a sign of dissecting aneurism Other signs may include the appearance of a nonpulsating mass in the inguinal region, ecchymoses over the abdominal wall, abnormal localized pulsations either on the anterior chest wall near the base of the heart, or in the interscapular region, the location of these pulsations shifting from day to day In addition, bizarre neurological signs may be present, and fever may develop

Pulsation of the right or left sternoclavicular joint may occur This is due to the sudden fluctuating increase in superior mediastinal pressure resulting from the acute expansion of the aorta When sternoclavicular pulsation occurs in association with aortic insufficiency, a dilated aorta and hypertension, a diagnosis of dissecting aneurism can be made with certainty

The Heart.—Moderate or marked enlargement of the heart may be present, due to the antecedent hypertension. However, not all patients have antecedent hypertension or enlargement of the heart.

On percussion, the area of dullness to the right and left of the sternum at the base is increased due to the widening of the aorta produced by the dissecting column of blood. An aortic systolic or diastolic murmur may appear (page 161) if the dissecting column of blood causes deformity or incomplete coaptation of the aortic valves. A friction rub may develop if rupture of the aorta occurs.

Fluoroscopic and X-Ray Examination.—Progressive widening or unusual, rapid, serial changes of the aortic shadow or its brachiocephalic branches, with diminished or absent aortic pulsations is the most characteristic *x*-ray finding. The esophagus and trachea may be displaced to the left by the widened aorta.

Angiocardiography may show a greatly widened aorta with a comparatively small lumen. A double-barrelled aorta, if present, can also be visualized.

Electrocardiogram.—No specific changes appear. However, the electrocardiogram may not be normal and may show ventricular strain or left bundle branch block due to the antecedent hypertension. If a coronary artery is occluded by the dissecting aneurism, myocardial infarction, with characteristic electrocardiographic patterns may develop.

Diagnosis.—The clinical picture of dissecting aneurism may be very similar to that of acute myocardial infarction. However, the wide distribution of pain progressing from thorax to the abdomen and back and then to the lower extremities, neurological disturbances, continued elevation of blood pressure or a rapid rise to a hypertensive level after the initial fall, and the absence usually of specific electrocardiographic changes in dissecting aneurism allow a differential diagnosis to be made in most cases. The diagnosis of a dissecting aneurism should be suspected when an aortic murmur suddenly appears in a patient with previous hypertension who develops severe substernal pain and collapse.

When a dissecting aneurism involves the common iliac arteries, it may simulate a saddle embolus of the abdominal aorta. However, in a saddle embolus, the pain first starts in the legs, whereas in dissecting aneurism, the pain is first noted in the thorax or lower back, and only later in the legs.

Course and Prognosis.—Death may occur instantaneously or in the course of a few hours or days from shock, rupture of the aorta, pericardial tamponade or from heart failure. However, the dissection may stop after the intima tears, or a double-barrelled aorta may result, and the patient may survive and live for many years.

Treatment.—There is no effective treatment for dissecting aneurism. In those cases who have survived, attempts have been made to wrap cellophane around the aorta, to prevent rupture.

DISEASES OF THE PULMONARY ARTERY

Some of the more common diseases affecting the main pulmonary artery are:

1. *Atherosclerosis of the Pulmonary Artery.*—This may occur independently of, or in association with, conditions producing hypertension of the pulmonary circulation (see Cor Pulmonale, page 635).

2 *Congenital Malformations of the Pulmonary Artery*.—These include communications between the aorta and pulmonary artery (page 470), transposition of the aorta and pulmonary artery (page 447), idiopathic dilatation of the pulmonary artery (page 451), pulmonary stenosis, either isolated or as part of the tetralogy of Fallot (pages 417 and 425), pulmonary artery dilatation associated with the Eisenmenger complex (page 412).

3 *Pulmonary Arteritis*.—This may occur in rheumatic fever, bacterial endocarditis, syphilis, *etc.*, but is of little clinical importance.

4 *Aneurism of the Pulmonary Artery*.

Aneurism of the Pulmonary Artery.—Aneurism of the pulmonary artery is comparatively rare Its etiology may be syphilitic, congenital, mycotic, arteriosclerotic and possibly traumatic. Congenital aneurisms of the pulmonary artery may be associated with a patent ductus arteriosus The aneurism may be saccular or fusiform.

Symptoms.—The most common symptoms are dyspnea, cough and hemoptysis There may also be chest pain.

Signs.—Abnormal dullness to the left of the sternum at the base may be present A systolic and even a diastolic pulmonary murmur may be present, due to concomitant stretching of the pulmonary valve ring. X-ray examination reveals a fusiform or saccular dilatation which is contiguous with the pulmonary artery shadow in all positions. A hilar dance (page 193) may or may not be present.

Diagnosis.—The diagnosis of aneurism of the pulmonary artery is difficult, because it may be simulated by an aortic aneurism or a mediastinal tumor. In addition, there are numerous conditions which can produce even marked dilatation of the pulmonary artery without aneurism formation These include congenital idiopathic dilatation of the pulmonary artery, patent ductus arteriosus, unequal division of the primitive truncus arteriosus, interauricular septal defects, the Eisenmenger complex, cor pulmonale, mitral stenosis, aortic-pulmonary fistulas, *etc.*

Course and Prognosis.—Death rarely occurs from rupture.

Treatment.—There is no effective treatment, although ligation of the aneurism has been attempted.

ANEURISMS OF VISCERAL AND PERIPHERAL ARTERIES

Aneurisms of Visceral Arteries.—Aneurisms may occur in the hepatic, renal, splenic and coeliac axis arteries, in addition to the abdominal aorta. Common causes of such aneurisms are mycotic embolic arteritis, periarteritis nodosa, and congenital weakness of the vessel wall.

Aneurisms of the Head.—Aneurisms of the cerebral arteries are usually found in the circle of Willis at the base of the brain and are usually congenital They may occur in association with coarctation of the aorta. They may rupture spontaneously producing a subarachnoid hemorrhage with sudden, excruciating headache, signs of meningeal irritation, abnormal reflexes which change daily, including a positive Babinski reflex, and bloody spinal fluid. The patient may lapse into coma In other cases, sudden death occurs Treatment is symptomatic.

Aneurisms of the Neck.—These are comparatively rare. The innominate artery (page 550), subclavian artery or carotid artery is usually involved Syphilis is a common cause of aneurism of the innominate artery. Trauma and arteriosclerosis more commonly affect the other vessels. The tortuous, buckled, right carotid artery which occurs in patients with hypertension and arteriosclerosis should not be mistaken for an aneurism (see page 148) A tortuous innominate artery may also occur in hypertension and simulate an aneurism

Aneurisms of Peripheral Arteries—Aneurisms develop in peripheral arteries especially where the artery is subject to repeated flexion Thus, common sites of peripheral aneurisms are the popliteal artery, the femoral artery in Scarpa's triangle, and the axillary and brachial arteries Common causes of peripheral aneurisms are trauma, mycotic embolic arteritis, as occurs in bacterial endocarditis, or mycotic arteritis from tuberculosis, actinomycosis, *etc*, periarteritis nodosa and other conditions producing a necrotizing arteritis, and congenital weakness of the vessel wall. Trauma often produces a false aneurism, where the entire vessel wall ruptures and the wall of the aneurism is formed by thickened connective tissue or an organized blood clot

Diagnosis of Peripheral Aneurisms.—An aneurism can usually be diagnosed by the presence of a pulsating, expansile mass, contiguous with the normal arterial pulsation A systolic thrill and bruit are usually present over the mass A diastolic thrill and murmur may also be present, but there is a pause between the systolic and diastolic components unlike the continuous murmur of an arteriovenous fistula

Course and Prognosis of Peripheral Aneurisms—A small aneurism often does not incapacitate the patient in any way However, rupture may occur, or the aneurism may press on a nerve trunk, producing severe pain or muscular paralysis

Treatment—Treatment is often unnecessary. However, if the aneurism expands and presses on a nerve trunk, or ruptures, it can be excised

ARTERIOVENOUS FISTULA

An arteriovenous fistula (*a-v* fistula, arteriovenous aneurism) consists of an abnormal, direct communication between an artery and a vein It may be congenital or acquired The acquired fistulas are usually due to trauma, such as bullet or stab wounds. Although arteriovenous fistulas may occur in any part of the body, they are usually found in the extremities between medium-sized arteries and veins, or in arteries and veins, such as the femoral and carotid vessels which are closely incorporated in a common sheath

Pathological Physiology.—Because of the arteriovenous fistula, blood is short-circuited from the artery directly to the vein without passing through the capillaries This causes a decrease in the total systemic resistance, an increased venous return, an increased pressure in the right auricle which in turn causes a tachycardia, an increased stroke volume and an increased cardiac output (the Bainbridge reflex) Eventually, the increased cardiac output may result in cardiac dilatation, hypertrophy and even in heart failure.

Marked peripheral vasodilatation also occurs, possibly as a means of dissipating the excess heat generated by the increased cardiac output and the increased bodily metabolism that results. A similar vasodilatation occurs in fevers, hyperthyroidism, beriberi, and severe anemias.

Pathology.—A portion of the artery proximal to the fistula is dilated. This arterial dilatation may extend back to the heart. *In addition*, an aneurism may spontaneously develop in the dilated artery just proximal to the fistula.

Distally to the fistula, the artery is smaller than normal, its pulse weaker and the circulation to the limb distal to the fistula impaired, so that ulceration and even gangrene *may occur.*

Varicose enlargement of the veins occurs especially in the neighborhood of the fistula, due to marked collateral circulation which develops at or proximal to the fistula. The collateral circulation may be *so great that the* surface temperature of the affected limb may remain higher than on the normal side ever after the fistula is excised.

Symptoms.—The patient may be aware of a pulsating mass or of a continuous bruit originating in the fistula. However, in many cases, the fistula itself is symptomless, and the patient's complaints, such as palpitation and dyspnea, are due to cardiac enlargement which has occurred.

Signs.—In the affected limb, the skin may be warm, and large, dilated superficial veins are often present. Palpation and auscultation over the fistula reveal a continuous thrill and a continuous machinery bruit, accentuated in systole

The systolic blood pressure is normal, but the diastolic pressure low due to the peripheral vasodilatation. The pulse pressure is therefore wide. Capillary pulsation (page 140), a collapsing pulse (page 140) and Duroziez' sign (page 144) may also be present as a result of the vasodilatation.

If the fistula is occluded by manual pressure, there is an immediate rise in systolic pressure In addition the pulse slows (Branham's bradycardiac reaction). Both of these phenomena persist for only a few seconds. The explanation for the rise in blood pressure is that with the closure of the fistula, the peripheral resistance is raised, since a large quantity of blood must now pass through the capillaries instead of through the shunt The drop in pulse rate is probably produced through reflex vagal stimulation as a result of a rise in the pressure in the aorta and the stimulation of vagal fibers embedded in the aortic wall. Therefore, if the patient is given a large dose of atropine, slowing of the pulse after compression of the fistula can often be abolished

The Heart.—Some degree of cardiac enlargement is present, although this may be minimal and is evident sometimes only by comparing *x*-ray films taken before and after development of the fistula (or by noting the decrease in heart size after excision of the fistula). A snapping apical first sound may be present, along with an apical or pulmonary systolic murmur. Signs of right- and left-sided heart failure may appear in long-standing cases, along with a diastolic gallop and even a diastolic apical murmur, such as occurs in cases of severe anemia, hyperthyroidism, beriberi, *etc*

Fluoroscopic and X-Ray Examination.—No characteristic findings are present in the heart.

Electrocardiogram.—No characteristic findings are present.

Laboratory Tests.—Circulation times are rapid The venous pressure is normal unless heart failure is present. The cardiac output is elevated, and the basal metabolic rate high Blood drawn from one of the veins near the fistula shows a higher oxygen content than normal

Diagnosis.—The finding of a continuous thrill and bruit in one of the extremities is characteristic of an a-v fistula However, a peripheral arterial aneurism can simulate a fistula because it may produce a systolic and diastolic thrill and bruit. However, in such cases, there is a slight pause between the systolic and diastolic phases, and commonly only a systolic bruit is present In addition, cardiovascular signs, such as tachycardia, decreased diastolic pressure, and Branham's bradycardiac reaction are absent

Course and Prognosis.—Cardiac enlargement eventually appears, depending on the location and size of the fistula Rarely, spontaneous healing occurs within six months. Complications, such as gangrene of the extremity distal to the fistula, may occur, as well as the development of an aneurism proximal to the fistula, with subsequent rupture Bacterial endocarditis may also engraft itself on the fistula

Treatment.—The fistula should be obliterated as soon as sufficient collateral circulation has developed to nourish the tissues This may take two or three months or more

Theoretically, some procedure, such as simple ligation of the fistulous tract, or lateral angiorrhaphy, both of which preserve the lumen of the affected artery and vein, is ideal. However, such procedures are often not possible, and quadruple ligation with excision of the fistula and the adjoining segments of artery and vein has been the operation of choice Recently, transvenous arteriorrhaphy, with closure of the fistula by suture and obliteration of the vein has been used

When the fistula is obliterated, the over-all resistance of the circulation is increased, putting an added strain on the heart This may lead to sudden heart failure and death Thus, it is advisable to perform a phlebotomy of from 500 cc to 1000 cc at the time of operation, especially in long-standing cases where the blood volume may be very high

CONGENITAL ARTERIOVENOUS FISTULA

Congenital arteriovenous fistulas are due to embryonic communications between arteries and veins which do not close Usually, there are numerous small communications between the artery and vein instead of one large communication These small, multiple communications may remain functionally closed even until after puberty If the fistula manifests itself in childhood, unilateral overgrowth of the affected limb may occur along with increased hair on the limb or increased sweating

Any region of the body may be affected, including the cerebral or pulmonary vessels. The clinical picture is similar to that of an acquired arteriovenous fistula, except in the case of a pulmonary arteriovenous fistula which is described below. However, enlargement of the heart does not occur in most cases of congenital arteriovenous fistulas because the volume of blood shunted through the fistula is usually very small; but if sufficient blood is

shunted through the fistula, cardiac enlargement and heart failure will occur even in a congenital fistula.

The congenital fistulas are often slow-growing and may never require surgical excision. If the fistula is in an extremity, the use of an elastic stocking or a pure rubber bandage is often very satisfactory.

CONGENITAL PULMONARY ARTERIOVENOUS FISTULA

The clinical picture of congenital pulmonary arteriovenous fistula (cavernous hemangioma of the lung, arteriovenous aneurism or varix of the lung) is more like that of a congenital cyanotic cardiac lesion than of an arteriovenous fistula

Pathological Physiology.—Because of the entrance of blood from the pulmonary arteries directly into the pulmonary veins, one would suppose that the venous return to the heart would be increased, resulting in an increased cardiac output and enlargement of the heart, as occurs in a systemic arteriovenous fistula. The reason that this does not occur in a pulmonary arteriovenous fistula is that the pulmonary resistance is ordinarily so low that even if it is lowered further by the fistula, it does not cause an increased venous return to the heart.

Since some of the unoxygenated blood passes directly through the fistula into the pulmonary veins and into the left side of the heart and to the systemic circulation without being oxygenated, the effective pulmonary blood flow is decreased and the systemic arterial blood becomes incompletely oxygenated. The situation is therefore similar to what occurs in the tetralogy of Fallot and in other congenital cyanotic lesions with *a-v* septal defects, and cyanosis, clubbing of the fingers and toes, and secondary polycythemia may occur

Pathology.—The fistula may be single, or multiple fistulas may be present The fistula consists of a mass of tortuous dilated pulmonary arteries and veins which compress the adjacent lung tissue. The actual fistulous connections are probably multiple and small and are difficult to demonstrate

Symptoms.—The cyanosis and polycythemia produce dyspnea, dizziness, faintness and thickness of speech Convulsive seizures may also occur. The increased vascularity of the affected lung may cause hemoptysis

Signs.—Cyanosis is present with clubbing of the fingers and toes. The plethoric appearance of polycythemia may also be present. In addition, more than half the patients show associated small capillary hemangiomas of the skin or mucous membranes (hereditary hemorrhagic telangiectasia, Rendu-Osler-Weber disease)

Examination of the chest usually reveals a vascular bruit over the affected lung. The bruit is usually systolic, rarely continuous. The heart is usually normal on physical examination.

Fluoroscopic and X-Ray Examination.—A characteristic nodular density (or densities) which may or may not pulsate, is present in the lung fields. The hilar markings on the affected side are prominent and show increased pulsations The density becomes larger during the Valsalva procedure and smaller during the Muller procedure. (The Valsalva procedure consists in

attempted forced expiration with the glottis closed, after a deep inspiration. The Muller procedure consists in attempted forced inspiration with the glottis closed, after a deep expiration.)

Electrocardiogram.—No significant findings appear

Laboratory Tests.—Polycythemia is present with a red blood count that varies from 6 to 8 million Prolonged arm-to-lung and arm-to-tongue circulation times have been reported with a marked increase in circulating blood volume. The venous pressure is normal

Diagnosis.—The clinical picture consists of cyanosis, clubbing of the fingers and polycythemia associated with a small heart and a nodular density in the lung fields It can be confused with primary polycythemia, or congenital heart disease of the cyanotic type

Course and Prognosis.—Death may occur from massive pulmonary hemorrhage or from a cerebral or cardiac complication of the polycythemia (page 727)

Treatment.—Local surgical excision of the fistula or lobectomy or pneumonectomy can produce a cure with regression of the symptoms and signs of cyanosis and polycythemia.

ARTERIAL EMBOLISM

The more common sources of arterial emboli are chronic auricular fibrillation with a thrombus in the left auricle, or myocardial infarction with a thrombus in the left ventricle, or bacterial endocarditis involving the mitral or aortic valve or a thrombus in one of the pulmonary veins Less common sources of arterial embolism are arterial air embolism (page 590), or tumor masses that invade the pulmonary veins, tumors of the left auricle or ventricle, syphilitic or atheromatous plaques of the aorta that break down, or a thrombus in an arterial aneurism or even a thrombus in a patent ductus arteriosus. Paradoxical arterial embolism can also occur from a venous thrombus in cases of auricular or ventricular septal defects or even with a patent foramen ovale (page 392)

Common sites of arterial embolism are the cerebral arteries, central retinal artery; internal carotid artery; coronary arteries, mesenteric, renal or splenic arteries, subclavian, axillary, brachial, radial or ulnar artery, aorta, iliac, femoral, popliteal, posterior tibial artery, *etc* The emboli usually occur at a point where the artery bifurcates because at this point the caliber of the vessel suddenly narrows

The symptoms and signs of embolism depend on the location of the embolus, its size, the artery occluded, and the degree of collateral circulation available Some of the more common manifestations of arterial emboli are as follows.

Cerebral Embolism.—This results in monoplegia, or hemiplegia, or aphasia or other neurological disturbances However, if the embolus is small, there may occur only a transient loss of consciousness, or an impairment of memory, slurring of speech, or other minor signs

Mesenteric Arterial Embolism.—This produces hemorrhagic infarction of the bowel Sudden generalized abdominal pain usually occurs with vomiting which may become intractable, and the patient may go into shock.

There may be some degree of abdominal rigidity or tenderness, and there is often marked distention The stool may be bloody, and a marked leucocytosis is characteristic, with the white blood count rising even to 35,000 The condition is serious and death often occurs even with surgical intervention

Embolism of the Spleen.—This produces marked left upper quadrant pain, fever and leucocytosis.

Embolism of the Kidneys.—Pain in the loins may or may not appear. However, microscopic or visible hematuria will develop.

Embolism of the Coronary Arteries.—See page 590.

Embolism of the Abdominal Aorta.—If the embolus lodges at the bifurcation of the aorta into the common iliac arteries (saddle embolus), the patient experiences sudden excruciating pain in the mid-abdomen or back, followed in a few minutes by a severe ache in one or both legs This is shortly followed by numbness and complete loss of sensation in the lower extremities Shock appears, and the lower extremities are found cold and pallid, with absent pulsations bilaterally from the femoral arteries down. Palpation of the abdomen reveals absent aortic pulsations below the umbilicus However, this is not diagnostic of a saddle embolus because normally the aorta *dips into the pelvis at about this level and no pulsations can be felt.* Gangrene of one or both legs usually appears within a few days and death shortly follows

A similar clinical picture may develop after embolism to the femoral or one of the more distal arteries, if the thrombus propagates upward into the aorta. In addition, primary thrombosis of the abdominal aorta may also produce a similar clinical picture However, in such cases, the occlusive process is so slow that sufficient collateral circulation develops to prevent gangrene even when the aorta is completely occluded (see page 671).

Embolism of the Arteries of the Extremities.—Diagnostically, arterial embolism to the extremities is characterized by the "five P's," namely, pain, pallor, pulselessness, paresthesia, and paralysis Later, gangrene of one or more digits or a portion of the limb may occur

Localization of the site of the embolus is often possible. The site of the arterial occlusion is just distal to the point where normal pulsations cease, but it is not possible to palpate most arteries along their entire course. However, marked tenderness is present at the point of occlusion The level at which the normal warmth of the skin changes to coldness also offers a clue to the location of the embolus. Thus, in occlusion of the popliteal artery, this level is located roughly just above the ankle In occlusion of the femoral artery where it bifurcates into the superficial and profunda branches, the level is at the juncture of the lower and middle thirds of the thigh When the common iliac artery is occluded, the level is at the juncture of the middle and upper thirds of the thigh.

The Diagnosis of Arterial Embolism.—Arterial embolism can be simulated by arterial thrombosis Thus, cerebral thrombosis, mesenteric arterial (or venous) thrombosis, thrombosis of the abdominal aorta or of the peripheral arteries, *etc.*, can produce the same clinical picture as embolism. There are, however, some points of differentiation:

Thrombotic processes, unlike embolism are often slow in developing, but *an embolus may occur without the sudden appearance of pain or the development of marked abnormal signs* Similarly, signs of an arterial thrombosis may appear with dramatic suddenness, and the differentiation between embolism and thrombosis may be difficult In this connection the etiology of arterial thrombosis may be of value Arterial thrombosis usually occurs as a result of arteriosclerosis, trauma, during an acute infectious disease, such as pneumonia, or during nonspecific infections such as chronic ulcerative colitis, or in the course of a local or generalized arteritis, such as occurs in lupus erythematosus or thromboangitis obliterans or periarteritis nodosa, during the course of severe heart failure, as a postoperative complication, as a result of blood dyscrasias, especially polycythemia, and finally thrombosis *may occur for no apparent reason*

Acute thrombophlebitis of the deep veins of an extremity can also simulate an embolus if generalized arterial spasm of the affected extremity occurs However, in such cases, some swelling of the extremity is present, and anesthesia and muscular paralysis do not develop

Course and Prognosis — This depends on the site of occlusion Saddle embolism of the aorta, mesenteric embolism, or embolism of the femoral artery or of other large arteries is very serious Cerebral embolism, or coronary artery embolism, itself need not cause death

Treatment.—The treatment of arterial embolism can be conservative (medical), or surgical

Medical Treatment —*It is generally agreed that arterial emboli to the* upper extremities, even if untreated, carry a better prognosis than those to the lower extremities However, regardless of the site of the embolus, the following procedures can be carried out

1 Opiates can be used to relieve pain

2 An attempt should be made to relieve the generalized arterial spasm which develops in the affected extremity Reflex heat to parts of the body other than the affected extremity is valuable For example, after an embolus to a lower extremity, hot water bottles can be applied to the lower abdominal wall or the small of the back However, heat should not be applied directly to the affected extremity The patient should also be kept in a *warm room*

3 Papaverine, 30 mg (½ grain) can be injected, if possible, into the arterial segment proximal to the embolus Thus, if a popliteal or tibial embolus is present, the intra-arterial injection would be made into the femoral artery A therapeutic response should be evident within a few minutes The injection can be repeated in several hours Intravenous or oral papaverine usually has little value in cases of embolism, and if the drug is used orally it should be given in doses of at least 0 1 gram (1½ grains) 4 times daily

4. *Alcohol, orally, in liberal doses,* has also been recommended for its general vasodilating effect Paravertebral block, or tetraethylammonium chloride intravenously, intermittent venous occlusion, and the use of an oscillating bed have also been used without any dramatic results

5 Heparin should also be used (page 606), because it will prevent the extension of the occlusive process in the artery In addition, even if embo-

lectomy is necessary later, it can be done without fear of hemorrhage. The heparin should be continued for about five to ten days. An alternate method is to use heparin for forty-eight hours and then continue with Dicumarol (page 605).

Surgical Treatment.—This consists of embolectomy. It should be done preferably within ten hours after the embolism occurs, because after this period the muscles die and the arterial endothelium will be so damaged that a new thrombus will form after the embolus is removed. However, embolectomy has occasionally been successful when done sixty or more hours after the embolism occurred. Heparin should be started at or immediately after the operation, to prevent thrombus formation within the sutured artery.

Embolectomy has been used in selected cases of embolism to the peripheral arteries of both the upper and lower extremities It should always be considered in cases of saddle embolism of the aorta, and in embolism of the common iliac or femoral artery. Popliteal embolectomy is not recommended because of the difficulty in removing the embolus without injuring collateral arteries. If gangrene has developed, embolectomy should not be done In such cases, amputation may be necessary, but a necrotic toe or toes may slough off spontaneously.

Regardless of whether medical or surgical therapy is used, it is still not possible to save every limb or every life The cause of death is not so much the peripheral embolism, but usually a later cerebral embolus or heart failure

Prophylactic Therapy—In patients with rheumatic heart disease, mitral stenosis and auricular fibrillation, who are throwing multiple systemic emboli from a thrombus in the left auricle, long-term anticoagulant therapy with Dicumarol has been used successfully Dicumarol or heparin is used in the treatment of acute myocardial infarction with a similar purpose in mind Here, arterial emboli may originate from a thrombus in the left ventricle

ARTERIAL THROMBOSIS

The most common cause of arterial thrombosis is atherosclerosis (page 581) Less frequently, it may be due to syphilitic endarteritis, to *infectious disease, to periarteritis nodosa or thromboangiitis* obliterans or to blood dyscrasias, such as polycythemia, which cause an increased coagulability of the blood

Thrombosis of the coronary arteries and myocardial infarction have already been described on page 593 Thrombosis of the pulmonary arteries has been described as a cause of pulmonary infarction However, I believe *that most if not all of these cases are due to pulmonary embolism.* Thrombosis of the arteries of the lower extremities is the most common cause of intermittent claudication. However, the diagnosis of peripheral vascular disease is outside the scope of this book

Two other less known forms of arterial thrombosis can be briefly described:

Thrombosis of the Internal Carotid Artery.—Most cases occur in the third to the fifth decade of life. Men are affected much more frequently

than women The left side is involved about seven times as often as the right The most common causes are atherosclerosis and thromboangiitis obliterans. Rarely, the syndrome is caused by an embolus from an atherosclerotic plaque arising lower in the aorta.

The onset of the illness occurs in one of three forms.

1. About 40 per cent of the cases have transient attacks of headache, hemiparesis, paresthesias and aphasias.

2 About 35 per cent of the cases have a sudden apoplectic onset with rapid loss of consciousness, hemiplegia or severe headache

3 The remaining 25 per cent of cases have a slowly progressive onset with severe headaches over a period of months, sporadic convulsive seizures, paresthesias and weaknesses which increase suddenly.

In any of these groups, ocular symptoms such as blindness in one eye or homonymous hemianopsia may occur

Diagnosis can be made by cerebral angiography. However, occlusion of the internal carotid artery can be detected by palpation of the artery through the pharynx in the following way (after Dunning):

The patient is placed in the supine position and requested to breathe through the mouth The examining physician, wearing a rubber glove moistened with water to minimize the friction that initiates the gag reflex, gently palpates the posterior wall of the pharynx with the forefinger and very slowly draws the finger laterally as far as the pharyngopalatine muscle When this muscle is relaxed, distinct pulsation of the artery can be felt more readily, while the thumb of the other hand is pressing externally in the carotid fossa If, after repeated trials, no pulsation is detected, it would seem safe to assume that the lumen of the artery is very narrow or nonexistent Palpation on both sides of the pharynx should always be carried out Clonic contractions of the pharyngopalatine muscle may simulate the pulse These contractions may be differentiated from pulsation of the internal carotid by timing them with the usually visible common carotid pulsation in the neck If repeated gagging occurs, the procedure should be terminated, because contraction of the pharyngopalatine muscle pushes the examining finger medially and covers the artery The palpation must be light and gentle, as too much pressure causes gagging It is not necessary to block the gag reflex by injecting cocaine into the pharynx

If the diagnosis is made early, the damaged segment of artery can be excised and anticoagulant therapy can be used

Thrombosis of the Bifurcation of the Abdominal Aorta (The Leriche Syndrome) —Severe atherosclerosis of the abdominal aorta may cause thrombosis and occlusion at the point where it bifurcates and forms the iliac arteries The thrombus may extend superiorly and involve the renal and superior mesenteric arteries During or after the gradual occlusion of the aorta, collateral channels develop, but eventually ischemia of the lower extremities becomes evident Rarely, it is produced by an arteriosclerotic or dissecting aneurism of the aorta, or by a neoplasm.

Symptoms.—The following symptoms occur most commonly: There is fatigue and pain low in the back, hips and thighs. This is particularly noticed on exercise and is a form of intermittent claudication This may be associated with coldness of the lower extremities Another symptom which often appears is impotence or inability to maintain an erection of the penis This is apparently due to an insufficient supply of blood to the cavernous structure of the penis.

Signs.—Arterial pulsations are not diminished nor absent in the abdominal aorta (see page 455) A systolic murmur may develop just to the left of the umbilicus

Bilateral femoral pulsations are absent and oscillometric readings of the lower extremities show no oscillations. However, a patient may occasionally develop weak unilateral or bilateral femoral pulsations. These are produced by very large anastomoses to the femoral artery.

Diagnosis.—Chronic obliteration of the abdominal aorta must be differentiated from other conditions in which the patient complains of easy fatigability of the legs, or intermittent claudication, and shows diminished or absent pulsations in the lower extremities. Coarctation of the aorta can be ruled out by the absence of rib notching, the presence of a normal aortic arch in the chest *x*-ray film, and *x*-ray demonstration of calcification of the abdominal aorta (Atherosclerosis with calcification of the aorta distal to the coarctation is relatively uncommon.)

In addition, pulsations of the abdominal aorta are weak or absent in coarctation The presence of hypertension in the upper extremities cannot be used as a point of differential diagnosis because it can occur in both conditions Rare cases of coarctation of the aorta occurring distal to the usual site, especially subdiaphragmatic coarctation can only be diagnosed by arteriography

An aneurism of the abdominal aorta can be palpated

A saddle embolus of the aortic bifurcation (page 668) produces symptoms much more rapidly

Arteriosclerosis obliterans in the legs may simulate thrombosis of the aortic bifurcation especially if both femoral arteries are involved, or if the iliac arteries are involved The exact diagnosis can be determined by translumbar abdominal aortography

Treatment—It is difficult to evaluate the results of treatment at this time The simplest treatment consists of bilateral lumbar sympathectomy to improve the circulation to the lower extremities When possible, the thrombosed portions of the terminal aorta and common iliac arteries should be resected and replaced with an arterial homograft This is desirable because otherwise the thrombus may continue to grow Thromboendarterectomy has also been used If gangrene occurs, amputation may be necessary

THE SUPERIOR VENA CAVAL SYNDROME

The superior vena caval syndrome can be produced by obstruction of the superior vena cava; or by rupture of an aortic aneurism into the superior vena cava (page 548) Common causes of the syndrome are bronchogenic carcinoma, mediastinal tumors (malignant or benign), aneurisms of the aorta, tuberculous, syphilitic or pyogenic chronic mediastinitis, or thrombosis or thrombophlebitis of the superior vena cava.

Pathology.—The obstruction of the superior vena cava may be due to external pressure from an aneurism or tumor, or from fibrotic constricting bands In other cases, malignant tumor cells have invaded and occluded the vessel. So-called primary thrombosis of the superior vena cava has also been reported.

Pathological Physiology.—The relation of the point of obstruction of the superior vena cava to the entrance of the azygos vein into the superior vena cava is important in determining the extent of the collateral circulation which develops. Normally, the azygos vein arises from the inferior vena cava at the level of the renal veins, or is formed by junction of the lumbar veins on the right side It passes through the diaphragm, ascends posteriorly to the root of the right lung and penetrates the superior vena cava immediately before the latter vessel pierces the pericardium The azygos vein receives blood from the hemiazygos vein, the accessory hemiazygos vein, the bronchial veins, and the anterior and posterior intercostal veins

When the obstruction of the superior vena cava is above the point where the azygos vein empties into it, blood from the upper half of the body

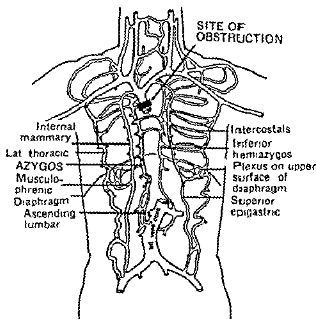


FIG 107 —Superior vena caval obstruction below (or including) the azygos vein The azygos vein and its tributaries show reversal of the blood flow, and all the blood returns to the heart through the inferior vena cava

reaches the right heart by collateral veins which drain principally into the azygos vein and from here into the unobstructed portion of the superior vena cava However, if the obstruction occurs at or below the point of entrance of the azygos vein, all of the venous blood from the upper half of the body must return to the heart through a circuitous route by way of the inferior vena cava Thus, blood from the subclavian, axillary and other veins in the upper half of the body pass through the lateral thoracic, thoracoepigastric, superficial epigastric, and superficial circumflex iliac veins into the long saphenous, the femoral veins, and into the inferior vena cava and the right heart Blood which enters the azygos vein must flow downward into the lumbar veins and the inferior vena cava instead of upward (Fig. 107)

Symptoms.—The increased venous pressure may cause fullness and flushing of the face and head, drowsiness, and occasionally convulsions. Dysphagia and hoarseness may be present as a result of the primary lesion. Dyspnea may also be present. The symptoms are alleviated by sitting or standing.

Signs.—Edema of the head and neck and upper extremities, and cyanosis especially of the head may appear. In addition, the superficial veins of the thorax and upper abdomen may become dilated and tortuous and fill abnormally from above, especially if the obstruction is at or below the entrance of the azygos vein. This can be demonstrated in the following way:

To test for reversal of blood flow in these veins, do the following: Choose a segment of vein where there are no side branches. Express the blood from it by means of two fingers pressed down on the vein together and then drawn apart, while maintaining pressure on the vein When a length of vein has been emptied in this way, lift one of the fingers off and note the time it takes the vein to refill. Repeat the above procedure, the other finger being taken off this time. It is generally easy to decide whether the vein fills from below upward, or from above downward

Normally, the blood in the superficial veins of the thorax and the upper abdomen fill from below upward Over the lower two-thirds of the abdomen, the veins normally fill from above downward. In superior vena caval obstruction, these conditions are reversed

Inspiratory filling of the neck veins may also appear if the obstruction is at or below the point of entrance of the azygos vein into the superior vena cava (see page 148) A positive hepato-jugular reflux is also present (page 110)

The heart is not affected by superior vena caval obstruction

Fluoroscopic and X-Ray Examination.—The heart is normal in size, but the shadow of the superior vena cava may be greatly widened

The collateral circulation can be well visualized by infra-red photography of the chest wall, or by angiocardiography which also demonstrates the obstruction of the superior vena cava.

Electrocardiogram.—The electrocardiogram is not affected

Laboratory Tests.—The venous pressure of the antecubital vein is elevated to 180 mm of water or more, but the venous pressure of the femoral vein is normal Similarly, arm-to-lung and arm-to-tongue circulation times are prolonged, but the thigh-to-lung and thigh-to-tongue times are normal.

Diagnosis.—The presence of cyanosis, edema and distention of the veins of the upper half of the body is characteristic of superior vena caval obstruction The clinical picture can be simulated by severe right-sided heart failure or constrictive pericarditis However, in both these conditions, there is also enlargement of the liver, and often ascites and edema of the lower extremities

Obstruction of the innominate vein (usually the left) produces swelling of the arm on one side and marked distention of the external jugular vein Obstruction of the subclavian vein produces only swelling of the arm

The exact location and the degree of obstruction can be determined by venograms done simultaneously in the antecubital veins of both arms.

Course and Prognosis.—The course and prognosis depend on the primary disease. Since malignancy and aneurism of the aorta cause the superior vena caval syndrome in over 70 per cent of cases, the prognosis is ordinarily poor However, in other cases, the patient may live for years in relative comfort.

Treatment —Symptomatic relief can be obtained by repeated phlebotomies. Surgical intervention can be used if the obstruction is due to external pressure or constrictive bands. Mediastinal decompression may be necessary in acute progressive superior vena caval obstruction

THE INFERIOR VENA CAVAL SYNDROME

The inferior vena cava in a normal person can be ligated without producing edema of the lower extremities (see page 128) However, occlusion of the inferior vena cava may occur as a result of thrombosis or thrombophlebitis, which either originates in the vena cava or extends from one or both femoral or iliac veins, or from external pressure due to ascites, neoplasms or constriction by fibrous bands, or occasionally from invasion of the vein by neoplastic tissue.

In any of these conditions a characteristic clinical picture may develop· Edema of both lower extremities usually occurs along with the development of dilated superficial varicose veins of the lower extremities and abdominal wall even extending to the thorax. The veins of the lower abdominal wall fill abnormally from below upward (see page 674) The venous pressure is characteristically elevated in the lower extremities but normal in the arms The heart is not affected. If the thrombosis extends upward to the renal veins, albuminuria, casts, and even hematuria may appear

Diagnosis.—Obstruction of the inferior vena cava can be simulated by chronic right-sided heart failure or constrictive pericarditis. However, the varicose veins of the lower extremities and the normal venous pressure in the arm differentiates obstruction of the inferior vena cava from these conditions In thrombosis of the portal vein, ascites occurs with gastric and intestinal hemorrhages, but the collateral circulation seen in obstruction of the inferior vena cava does not appear

Treatment.—There is no effective treatment for obstruction of the inferior vena cava The patient can get symptomatic relief by keeping the lower extremities elevated as much as possible or by the use of elastic bandages

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Chapter 43

THE HEART IN ENDOCRINE DISEASES. HYPERTHYROIDISM AND HYPOTHYROIDISM

HYPERTHYROIDISM

HYPERTHYROIDISM (thyrotoxicosis), either due to Graves' disease with diffuse hyperplasia of the gland, or to a toxic adenoma of the thyroid, may produce cardiovascular abnormalities, such as paroxysmal or persistent auricular fibrillation, or heart failure, or even *a-v* block, or may greatly *aggravate a pre-existing cardiac condition* The term *thyrocardiac, or thyroid* heart has been used for patients with hyperthyroidism who have auricular fibrillation, enlargement of the heart or signs of congestive heart failure

Pathological Physiology and Pathology.—The most common cardiovascular manifestations of hyperthyroidism are an increase in cardiac output, and *the development of auricular fibrillation. Hyperthyroidism can increase* the cardiac output in the following ways:

1 The marked rise in the metabolic rate which is characteristic of hyperthyroidism produces a marked increase in cardiac output which is accomplished mostly by an acceleration of the heart rate rather than by an increase in stroke volume Not only does the cardiac output increase but it becomes excessively great because energy is wasted in dissipating the excess heat which is produced Much of this heat is dissipated through the skin which becomes warm The skin vessels also become markedly dilated as a result of the great increase in peripheral blood flow

It has been found that if the metabolic rate of a normal person was increased to 100 per cent by exercise, the cardiac output increased only 85 per cent, but in a patient with hyperthyroidism due to Graves' disease, and a basal metabolic rate of + 100 per cent, there was an increase of 132 per cent in the cardiac output. Another factor which increases the heart rate and the cardiac output in hyperthyroidism is the effect of thyroxine directly on the cardiac muscle

2. Because of the excess heat production, marked peripheral vasodilatation occurs as I mentioned above This produces an increase in the venous return and a rise in cardiac output The venous return is further increased because the circulating blood volume is greater than normal

Because of the marked increase in cardiac output, it might be expected that the heart would dilate and hypertrophy, and eventually fail. However, this has been questioned by some investigators One reason for the confusion is that death usually occurs only after the hyperthyroidism has been present many years, and that many patients with hyperthyroidism have coincidental hypertensive, rheumatic or coronary artery lesions The consensus of opinion seems to be that while slight or moderate cardiac

dilatation can occur as a result of uncomplicated hyperthyroidism, extreme degrees of cardiac enlargement are probably always due to other coexisting cardiac lesions. Hyperthyroidism causes no specific lesions in the heart muscle, contrary to the opinion of early investigators

The mechanism by which hyperthyroidism produces auricular fibrillation is not known Auricular fibrillation has been precipitated in hyperthyroid patients by the injection of mecholyl (acetylbetamethylcholine chloride), and it has been noted that when mecholyl is injected into normal people it produces symptoms similar to those which occur as part of the hyperthyroid picture, namely, a tachycardia with visible blushing of the skin of the head and trunk and extremities (with the exception of the hands and feet), marked perspiration, a tremor of the hands and sometimes of the head, and even a marked rise in basal metabolic rate When mecholyl is given to hyperthyroid patients, it greatly aggravates their symptoms

Symptoms.—Many of the symptoms of uncomplicated hyperthyroidism are similar to those which occur in neurocirculatory asthenia, especially nervousness, palpitation, breathlessness and dyspnea, and precordial pain The palpitation which is usually due to the rapid heart rate may occasionally be produced by paroxysmal auricular fibrillation or flutter The dyspnea which is often of the sighing type (page 119) may actually be due to a slightly decreased vital capacity resulting from muscular weakness, and the great demands for oxygen required by the body In addition, the onset of left-sided heart failure aggravates the dyspnea

Although the precordial pain is usually functional in origin it may become severe during an attack of paroxysmal auricular fibrillation In addition, patients with hyperthyroidism may suffer from true angina pectoris, made worse by the hyperthyroidism Weakness may be marked This is actually due to a true muscular dystrophy produced by the hyperthyroidism It can be demonstrated by having the patient sit in a chair and hold a leg out as long as possible The patient with hyperthyroidism can do this for a much shorter time than a normal person The patients prefer cold weather to hot, have a tendency to diarrhea, and have an excellent appetite despite the fact that they may lose weight

Signs —Characteristic signs are often present The patient is very alert, has a quickness of motion, a warm, moist skin, excess perspiration, tremor of the hands and tongue, and exophthalmos and associated eye signs (page 145) if Graves' disease is present However, these signs may be minimal and are easily overlooked, especially if severe heart failure is present

Examination of the thyroid may disclose a diffusely enlarged gland with a characteristic bruit (page 147) However, the hyperthyroidism may be produced by a toxic adenoma which may be almost too small to palpate

The Pulse and Blood Pressure.—A sinus tachycardia is usually present with a rate around 120, but it may be much faster or much slower An interesting feature of the heart rate is that it tends to remain elevated during sleep, unlike the sinus tachycardia of normal people, which disappears during sleep A collapsing pulse (page 140) may be present, because of the marked peripheral vasodilatation, along with Duroziez' sign (page 144) and a pistol shot sound in the femoral artery When auricular fibrillation is present, the apical rate tends to remain rapid, and is very refractory to digitalis.

The blood pressure may be normal or there may be a slight systolic hypertension The diastolic pressure remains normal or may be low because of the peripheral vasodilatation, producing a wide pulse pressure.

The Heart.—Physical examination discloses no enlargement of the heart in uncomplicated hyperthyroidism However, the apical impulse is very forceful and snapping, and on palpation, imparts the suggestion of a systolic thrill to the hand (page 155) A loud snapping first sound is present at the apex and it may simulate the presystolic murmur of mitral stenosis (page 157) A normal apical systolic murmur may be present, due to the rapid heart rate, and a normal pulmonary systolic murmur may appear, due to pulmonary artery dilatation A pulmonary friction rub may also occur, due to the dilated pulmonary artery rubbing against the pericardium (page 161).

Fluroscopic and X-Ray Examination.—No characteristic findings appear except that the pulmonary artery segment is accentuated, and the amplitude of cardiac pulsations is marked, due to the forceful heart beat.

Electrocardiogram.—There is no characteristic pattern. Large *T* waves have been reported. Sinus tachycardia is usually present. Paroxysmal or persistent auricular fibrillation is common; auricular flutter may occur, and rarely, incomplete or complete *a-v* block appears

Laboratory Tests.—The basal metabolic rate is characteristically elevated With moderate hyperthyroidism, the rate may vary from + 40 to + 60 per cent In severe cases, the rate may reach + 125 per cent.

Other laboratory tests helpful in diagnosis include the blood cholesterol level, which is often less than the minimal normal value of 150 mg. per cent However, it may be normal or even elevated, especially if coincidental hypertensive heart disease or coronary artery disease is present

A more exact test for hyperthyroidism is the determination of the precipitable or protein-bound iodine in the serum, because this is an index of the amount of circulating thyroid hormone present. Abnormally high values are found in hyperthyroidism. (Normal values are from 4 to 7 micrograms per cent) However, the determination of protein-bound iodine is a difficult and arduous technical procedure.

Protein-bound iodine levels are unreliable in any patient who has ever had a sinus tract injected with iodized oil (lipiodol), and in any patient who has ingested gallbladder dye within six months preceding the test. False values will also occur for a few days after an intravenous pyelography.

The uptake of radioactive iodine is probably the most accurate test of thyroid activity. A tracer dose of 100 microcuries of I^{131} is given orally. In a normal person, the uptake of the radioiodine by the thyroid is from 15 to 30 per cent (possibly 10 to 40 per cent) in twenty-four hours. The radioiodine which is not taken up by the body is excreted in the urine In patients with hyperthyroidism, 40 per cent or more of the iodine is picked up by the thyroid. In hypothyroidism, 10 per cent or less of the iodine is taken up by the thyroid.

Because of the increased cardiac output, both the arm-to-lung and arm-to-tongue circulation times are shortened The arm-to-lung time is usually four seconds or less The arm-to-tongue time is below ten seconds Even in cases where heart failure develops, the arm-to-tongue time seldom ex-

ceeds thirteen seconds. However, these short values are not pathognomonic of hyperthyroidism and occur in anemia, fever or in any condition with an increased cardiac output and peripheral vasodilatation (see page 221) The venous pressure remains normal unless right-sided heart failure occurs

Transient glycosuria may also occur

Diagnosis.—The diagnosis of uncomplicated hyperthyroidism with its classical signs is simple However, difficulty in diagnosis occurs when the symptoms and signs of mild hyperthyroidism are masked by those of cardiac decompensation. In such cases, warm moist hands, a history of marked loss of weight without anorexia, *etc*, are suggestive of hyperthyroidism, especially if the examination reveals no hypertension, valvular disease, or severe anemia. A history of multiple attacks of paroxysmal auricular fibrillation is also suggestive of hyperthyroidism, although this can occur in otherwise normal people. A short arm-to-tongue circulation time in the presence of left-sided failure is also suggestive. An elevated basal metabolic rate is not significant in the presence of left-sided heart failure, which itself can raise the metabolic rate even to + 60 per cent (page 242).

Occasionally, the symptoms of a pheochromocytoma (page 701) are suggestive of hyperthyroidism

Course and Prognosis.—Severe hyperthyroidism if left untreated often leads to auricular fibrillation, heart failure and death, especially if coincidental heart disease is present Occasionally hyperthyroidism spontaneously disappears.

Treatment.—Hyperthyroidism, even if uncomplicated, should be vigorously treated, and where hyperthyroidism is complicated by heart failure, both the heart failure and the hyperthyroidism should be treated simultaneously Medical, surgical or radiation therapy can be used.

General Supportive Measures.—Most patients with severe hyperthyroidism also suffer from general malnutrition, and specifically from a vitamin B complex deficiency, which may be one of the factors in causing heart failure In addition, there is usually some degree of liver damage present Therefore, a high caloric diet, of from 3000 to 5000 calories, with a high carbohydrate content, should be prescribed In addition, 50 to 200 mg. thiamin, 45 mg riboflavin, and 75 mg nicotinamide should be given daily With marked inanition it may be necessary to start with parenteral protein hydrolysates. Psychotherapy should also be instituted as quickly as possible to determine and alleviate the psychogenic factor which led to the onset of the disease

Thiouracil and Its Derivatives—Thiouracil and its derivatives, the least toxic of which are propylthiouracil and methylthiouracil apparently act by preventing the formation of thyroxin in the thyroid gland They do not interfere with the action of thyroxin on the tissues, so that in cases of hyperthyroidism with intractable exophthalmos, thyroxin or thyroid hormone can be given along with the uracil compounds.

Propylthiouracil can be given orally in the form of 50 mg tablets Initially, 50 mg can be given 3 times a day. This dose can be maintained until all signs and symptoms of the disease have been brought under control. *This may take three weeks or more, the basal metabolic rate falling about 1* per cent daily. Occasionally it may be necessary to use 300 mg or more to

alleviate the hyperthyroidism. The daily maintenance dose varies from 50 to 75 mg It should be continued for at least six months. A relapse may occur even in as high as 50 per cent of the cases after the drug is stopped However, another course of therapy can then be started.

If necessary, the drug can be continued indefinitely, for years.

A toxic depression of the white blood cells is rare with propylthiouracil but it may occur Therefore, a white blood count should be done weekly for the first six weeks, and every two weeks thereafter. However, if toxicity has not developed in six weeks, it probably will not occur later. The drug should be stopped if the white blood count falls below 4500, or if the granulocytes are reduced to 45 per cent or less. If after a few days, the white count begins to rise, the drug can be continued cautiously. Other signs of toxicity include sore throat, malaise, a drug fever or drug eruptions. Myxedema can be *induced if too much of the drug is given.* This disappears when the drug is stopped.

Methylthiouracil and other thiouracil derivatives have an action similar to that of propylthiouracil.

I believe that propylthiouracil is the drug of choice in the usual case of hyperthyroidism The special indications for surgery and for radioiodine therapy are discussed below

Radioactive Iodine (radioiodine).—The radioactive isotope, I^{131}, with a half life of eight days, administered orally with or without a small carrier dose *of stable iodine, is the iodine isotope now most generally used* It produces internal radiation by emitting beta and gamma rays, and results in marked fibrosis of the gland

A single dose of from 6 to 8 millicuries can be given, depending on the size and weight of the thyroid gland No further therapy with radioiodine should be given for about six to eight weeks, because it takes this time for the full therapeutic effect to occur, although clinical improvement usually can be noticed within a month. After six or eight weeks, another dose of radioiodine can be given, depending on the clinical picture.

If rapid clinical improvement is desired, supplementary ordinary iodides or propylthiouracil can be given, beginning ten days after the radioiodine. However, ordinary iodides should be withheld for several weeks before treatment with radioiodine to insure an adequate uptake of the radioiodine by the thyroid gland.

One difficulty with the therapeutic (or diagnostic) use of radioactive iodine is that its preparation and handling require specially trained personnel, elaborate safety precautions, and expensive physical equipment. In addition, it can produce myxedema, radiation tracheitis and esophagitis, *and may aggravate the ocular signs of hyperthyroidism.* However, it has been used successfully in up to 90 per cent of cases.

There is always the possibility that a thyroid carcinoma may develop years after radioactive iodine is used therapeutically. For this reason, it should not be used in a young person, but reserved for patients whose life expectancy is not more than twenty-five years It should not be used where there is a possibility of cancer of the thyroid, as in cases of toxic nodular goiter. Furthermore, such cases do not respond well to radioiodine, and the nodules frequently persist in spite of repeated doses.

Radioiodine, however, is the treatment of choice in a patient who has had a recurrence of hyperthyroidism after one or more thyroidectomies

Thyroidectomy.—Although subtotal thyroidectomy was the treatment of choice for many years, it is not completely curative, and recurrences may occur in as much as 10 per cent of cases, there is an operative mortality, which may approach 5 per cent in thyrocardiacs, and intractable exophthalmos may occur postoperatively

Preoperative therapy with either ordinary iodides or propylthiouracil is necessary to decrease the vascularity of the gland, and to lower the metabolism and enable the patient to withstand the operation better. Two hundred mg. propylthiouracil can be given daily, or a saturated solution of potassium iodide, 15 drops, 3 times daily It may require two or more weeks before the basal metabolism falls sufficiently to permit operation.

The most serious complication of thyroidectomy is a thyroid crisis It begins within the first twenty-four hours after operation and is characterized by the development of intense restlessness and agitation, which may lead to delirium The skin is flushed, and perspiration is profuse. The temperature rises rapidly even to 106°, nausea and vomiting may be present, and collapse and death may occur Treatment consists of morphine, oxygen, rapid digitalization, along with intravenous infusions of glucose in distilled water to restore the fluid loss Iodides in large doses (Lugol's solution, 4 cc every two hours) should be given orally or even intravenously if the patient is vomiting continuously Fortunately, with proper preoperative management, a thyroid crisis postoperatively is uncommon The crisis may also occur in patients who have not been operated on.

Other complications of thyroidectomy include the development of postoperative tetany if the parathyroid glands have been accidentally removed, or hoarseness due to accidental injury to the recurrent laryngeal nerves, or myxedema if too much thyroid tissue is removed

Surgery is the treatment of choice in all patients in whom there is a reasonable suspicion of carcinoma, in all who have discrete adenoma of the thyroid, because of the increased propensity to carcinoma, and in those in whom it is desirable to remove a large mass of nodular thyroid tissue for cosmetic reasons, or because of intrathoracic extension with pressure symptoms severe enough in themselves to require relief

If hyperthyroidism is complicated by heart failure, the failure should be treated in the usual way, including the use of digitalis Auricular fibrillation usually spontaneously disappears with medical or surgical or radiation therapy However, if it continues for two weeks postoperatively or after the metabolism has returned to normal, quinidine can be used to restore normal sinus rhythm (page 368) All signs of heart failure may disappear once the metabolism returns to normal In such cases, digitalis and other cardiac therapy can be stopped However, a mild or moderate degree of failure may persist, due to coincidental heart disease

HYPOTHYROIDISM AND MYXEDEMA

Moderate hypothyroidism may occur without any marked cardiovascular abnormalities. However, severe hypothyroidism in adults produces the

clinical picture of myxedema, and in children, cretinism. In both these conditions, the following cardiac abnormalities may appear, which have been described under the term, myxedema heart: There is a marked increase in the area of cardiac dullness on percussion, faintness of the heart sounds on auscultation, a markedly increased cardiac silhouette with feeble pulsations on fluoroscopy, flat or inverted *T* waves in the standard leads of the electrocardiogram, and a complete return of these abnormalities to normal after treatment with thyroid hormone. Although these and other abnormal cardiovascular signs appear in 75 per cent or more of patients with myxedema, there has been much confusion in the past as to their significance. However, recent observations indicate that these signs are due to the presence of marked pericardial effusion rather than to intrinsic disease of the heart. This will be discussed below.

Pathological Physiology and Pathology.—The basic physiological disturbance in myxedema is a very low basal metabolic rate. Inasmuch as the metabolic needs of the body are diminished, the cardiac output, the velocity of the blood flow, and the circulating blood volume also decrease. The slow blood flow enables the tissues to remove an increased volume of oxygen from the capillaries so that the arterio-venous oxygen difference increases This also allows the heart to perform less work, and as a result, the myxedematous patient can perform work using less energy than even a normal person This is in marked contrast to the conditions existing in hyperthyroidism where much energy is wasted. Because of the decreased metabolic needs of the body, and the low cardiac output, the pulse rate is also slow The circulation time becomes prolonged because of the decreased velocity of blood flow. The skin vessels remain contracted and the peripheral blood flow is also low as a means of conserving heat.

In addition to these cardiovascular disturbances, abnormalities in metabolism occur For example, the blood cholesterol level may rise to more than 600 mg per cent. In association with this, patients with myxedema appear to be particularly prone to atherosclerosis, especially of the coronary arteries, so that angina pectoris and myocardial infarction are frequently observed The bone marrow may be depressed, resulting in a hyperchromic anemia Another disturbance in metabolism causes the accumulation of a semi-fluid albuminous material in the skin which results in a nonpitting edema. A marked increase in capillary permeability also occurs and can result in massive pericardial effusion, ascites, and even in a *pitting edema* of the skin. Recent observations indicate that a pericardial effusion occurs in almost all cases of myxedema where the heart appears to be enlarged on *x*-ray examination The pericardial effusion is noninflammatory, although the fluid may have a high specific gravity and a high protein content, due to the increased capillary permeability.

The findings in the heart muscle may vary, and hydropic vacuolization, loss of striation and irregularity in the staining properties of the muscle fibrils have been noted along with an interstitial edema of the muscle fibrils. The predilection of myxedema for the development of coronary atherosclerosis and myocardial infarction has already been mentioned.

Symptoms.—The symptoms are essentially those of decreased thyroid activity and not of heart disease, and include easy fatigability, lethargy,

intolerance to cold, loss of hair, anorexia and constipation Dyspnea on exertion may occur along with a diminished vital capacity The decreased vital capacity is probably due to the fact that the low metabolic rate requires decreased respiratory activity. Angina pectoris may be present due to associated coronary artery disease. Symptoms of pericardial tamponade do not appear, due to the fact that the pericardial effusion develops so slowly, that the pericardium is able to stretch sufficiently to accommodate the fluid. Psychotic symptoms are also common.

Signs.—The patient presents an apathetic appearance with sluggish movements Obesity may or may not be present. The facial expression is often mask-like, the features coarse and the eyelids puffy Pallor may be marked and there may even be a malar flush The hair of the head, eyelashes, and eyelids is coarse, brittle and scant, and falls out easily The skin is dry and scaly and feels indurated, due to a non-pitting edema, most marked in the hands, feet and the supraclavicular fossæ However, a pitting edema may also be present The neck veins may or may not be distended The pulse is usually slow, and the blood pressure a low normal with a small pulse pressure, although occasional cases of myxedema with hypertension have been reported

Ascites or pleural effusion may be present

The Heart.—Signs of pericardial effusion are often present, including a weak apical impulse, a marked increase in the area of cardiac dullness and flatness, and faint heart sounds (page 644)

Fluoroscopic and X-Ray Examination.—The enlargement of the cardiac silhouette and the fluoroscopic findings are due to pericardial effusion (page 645). However, it is possible that slight enlargement of the heart may occur due to edema of the muscle fibers

Electrocardiogram.—The typical *T* wave patterns of pericarditis are usually present (page 645). However, these changes are not pathognomonic either of pericarditis or myxedema and may occur in beriberi, chronic nephritis and many other obscure conditions Abnormal *Q* waves and *RS–T* deviations, due to recent or old myocardial infarcts may also be present

Laboratory Tests.—The basal metabolism may vary from about −20 per cent to −40 or −45 per cent It does not become less even with complete absence of the thyroid The blood cholesterol level varies from about 400 mg to over 600 mg per cent. However, it may be normal

The venous pressure may or may not be elevated in spite of the pericardial effusion Arm-to-tongue circulation time may be prolonged to as much as twenty-five or thirty seconds in the absence of signs of left-sided heart failure The arm-to-lung time is also prolonged

Diagnosis.—When the heart is enlarged and the typical clinical signs of myxedema are present, diagnosis is easy, although one should remember that part of the cardiac enlargement and the abnormal signs may be due to coincidental heart disease and heart failure. However, myxedema should be suspected if marked cardiac enlargement or pericardial effusion occur especially in a woman, without any obvious cause A low basal metabolic rate, high blood cholesterol and a rapid clinical response to thyroid therapy confirm the diagnosis

The clinical picture and cardiovascular signs of myxedema may appear regardless of whether the myxedema has occurred spontaneously, or is the result of total surgical ablation of the thyroid gland, or of excess fibrosis due to radiation, or even if the myxedema is secondary to pituitary disease

Beriberi can sometimes simulate the clinical picture of myxedema, and in patients who do not improve with thyroid therapy, high doses of vitamin B can be tried

Course and Prognosis.—The untreated patient may live a semi-invalid life for many years. Death may occur from myocardial infarction or intercurrent infection. Although heart failure may occur in a patient with myxedema, it is probably due to coincidental cardiac disease. However, some cardiologists believe that heart failure occurs frequently as a direct result of the myxedema.

Treatment.—*The specific treatment of myxedema is the use of thyroid* hormone Dessicated thyroid substance is usually given orally, but should be used in small doses, because a rapid increase in metabolic rate may produce or aggravate angina pectoris, or precipitate a myocardial infarct. The dose of thyroid varies with the potency of the preparation used I have found Armour's thyroid substance satisfactory Therapy can be begun with a small daily dose varying from 15 to 30 mg. ($\frac{1}{4}$ to $\frac{1}{2}$ grain) The dose can then be increased weekly Usually not more than 30 mg. ($\frac{1}{2}$ grain) is necessary as a maintenance dose, although some patients may require as much as 180 mg (3 grains) daily.

Therapy can be guided by the return of a feeling of well-being, a rapid decline in the size of the heart, a fall in blood cholesterol level, a return of the *T* waves to normal, and a rise in the basal metabolic rate Marked clinical improvement occurs in a few weeks, before the basal metabolic rate returns to normal. Thyroid therapy must be continued indefinitely.

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Chapter 44

THE HEART IN ENDOCRINE DISEASES (*Continued*)

DISEASES OF THE PANCREAS

Diabetes Mellitus.—Although diabetes does not cause heart disease, hypercholesterolemia and atherosclerosis of the coronary arteries, and arteriosclerosis of the peripheral arteries are common and may appear at a relatively early age.

In uncomplicated diabetes, the electrocardiogram is normal, but *RS-T* deviations and flat or reversed *T* waves and a prolonged *Q-T* interval may occur transiently as a result of insulin administration. These changes are similar to, but more marked than those induced by eating and are related to the decrease in blood potassium which insulin produces (see page 716).

Similarly, electrocardiographic changes occur in diabetic coma, where the blood potassium may be very low as a result of excess vomiting. The electrocardiographic changes, however, are apt to be more marked while the patient is emerging from coma and is receiving treatment, because the large quantities of insulin and glucose used cause a further decrease in blood potassium, and it may be necessary to give potassium salts orally (5 to 10 grams of a 50 per cent solution of potassium chloride) or even intravenously (2 grams—100 cc of a 2 per cent solution) to prevent severe paralysis due to hypopotassemia (also see page 717). The above doses may have to be repeated.

In patients with diabetes and coronary artery disease, insulin should be used cautiously, and the urine should not be allowed to become sugar-free, because cases have been reported in which severe anginal attacks or even myocardial infarction have occurred as a result of excess insulin administration.

The Kimmelstiel-Wilson Syndrome.—This condition generally occurs in patients over fifty years, with long-standing but usually mild or moderate diabetes, severe and widespread edema of the nephrotic type, gross albuminuria and hypertension. Microscopically, the kidneys show a characteristic hyaline thickening of the intercapillary connective tissue of the glomerulus (intercapillary glomerulonephrosis). Diabetic and hypertensive retinopathy and characteristic doubly-refractile fatty cells or casts in the urine are also present.

Although the edema is usually described as nephrotic in type, right-sided heart failure is often present in these patients and contributes to the severity of the edema. The most common causes of death are uremia and heart failure. The heart failure should be treated according to conventional methods, and if hypoalbuminuria or anemia is present due to the renal lesion, these should be corrected if possible.

Hemochromatosis.—In hemochromatosis, there is, in addition to diabetes, cirrhosis of the liver and the deposition of iron-containing hemosiderin and other pigments in the skin and organs, including the heart. The heart muscle may also show degenerative changes. Some cases have developed heart failure, but the exact relation of the heart failure to the hemochromatosis is not known. A-V block has also been found in some cases.

DISEASES OF THE ADRENAL CORTEX

Introduction.—The adrenal cortex has a variety of functions, about which much is still unknown. So far, thirty steroid hormones have been isolated from the cortex. Of these, six are capable of maintaining life in an adrenalectomized animal. Although there is considerable overlapping of their functions, the adrenal cortical hormones can be divided into three groups with reference to their physiological activity.

1. *Electrolyte-controlling Steroids* (Salt hormones).—These include hormones such as desoxycorticosterone, and the newly discovered aldosterone (electrocortin). They work by promoting the reabsorption of sodium in the renal tubules and causing a retention of sodium and water in the body. In addition, they facilitate the urinary excretion of potassium and can cause hypopotassemia. There is no way as yet of directly measuring the activity of hormones of this group.

2. *Glycogenic Steroids* ("S" hormones).—These include corticosterone, cortisone (compound E) and the more important hydrocortisone (compound F). These hormones are commonly called the 11-oxysteroids, because of the presence of an oxygen at carbon 11. They work by causing the breakdown of protein into carbohydrate (gluconeogenesis). This can be seen in many ways. If it occurs in muscle, it causes muscular weakness. If it occurs in bone, it will cause osteoporosis and demineralization. It is also the cause of the negative nitrogen balance and skin abnormalities such as thinning of the skin, striæ and easy bruising.

In addition, these hormones raise the blood sugar level, fill the liver with glycogen, and impair glucose tolerance. The glycogenic steroids also cause a lysis of fixed lymphatic tissue and a decrease in circulating lymphocytes, and an almost complete disappearance of eosinophiles from the circulating blood.

The glycogenic hormones are excreted in the urine as glycogenic corticoids and can be measured qualitatively. The average daily excretion of the glycogenic corticoids is approximately from 25 to 75 units.

3. *Sex Steroids* ("N" hormones).—These include androsterone, which exerts an effect similar to that of the testicular androgens. As a result, masculinization can occur. In addition, these hormones also have an anabolic effect and build up tissue protein with the retention of nitrogen, phosphorus, potassium, sodium and chloride.

The sex steroids are excreted in the urine in the form of 17-ketosteroids, which are break-down products of the hormones. Average values for the daily excretion of the 17-ketosteroids in terms of equivalents of androsterone are as follows: children under six years of age, less than 1 mg.; adult women, 8 to 15 mg.; and adult men, 10 to 20 mg.

It has recently been suggested that only aldosterone, corticosterone and hydrocortisone are true secretions of the adrenal cortex and that the other steroids mentioned above are either metabolites or precursors of these three.

Recent studies have indicated that adrenal cortical function is regulated mainly through the anterior pituitary gland. This regulation is achieved through the secretion of the pituitary adrenocorticotrophic hormone (ACTH) The sequence is: stimulation of the anterior pituitary, release of ACTH, which stimulates the adrenal cortex, and finally the outpouring of the adrenal cortical steroid hormones

Hyperfunction of the Adrenal Cortex

Hyperfunction of the adrenal cortex, due to cortical tumors or to cortical hyperplasia may result in excess secretion of hormones, such as androsterone, which contribute to secondary male sex characteristics, and thus produce precocious sexual development in young boys of the masculine type, precocious sexual development in young girls, also of the masculine type, although homologous sexual precocity with uterine bleeding and enlargement of the breasts may also occur. In adult men, sexual changes are rarely observed because a masculinizing tumor is not likely to enhance the masculinity of a male, while feminizing tumors in adult males are very rare In adult women, masculinizing changes, such as amenorrhea, hypertrophy of the clitoris, alopecia of the scalp with hirsutism and acne of the face, extremities, chest and lower abdomen, and reversion to a masculine type of breast, are common. This tendency to masculinity has been described as the "adrenogenital syndrome" In these cases, the 17-ketosteroid excretion is very high, but no cardiovascular abnormalities result. However, when the hyperfunctioning cells are associated with an increased secretion of the glycogenic steroids, the clinical picture of Cushing's syndrome appears.

Cushing's Syndrome.—It is now generally believed that all patients with Cushing's syndrome have hyperadrenocorticism with excess production of the glycogenic corticoid steroids In most cases, Cushing's syndrome is due to adrenal hyperfunction with or without hyperplasia of the adrenal gland In other cases, a benign or malignant adrenal cortical tumor is present Rarely, the initiating cause of the syndrome is a basophilic tumor of the pituitary, or a masculinizing tumor of the ovary, such as arrhenoblastoma, or a granulosa cell tumor of the ovary, or a tumor of the thymus, or an intracranial lesion such as a pinealoma, or internal hydrocephalus. It is probable that in all these conditions the clinical picture is due to stimulation of the adrenal cortex by the pituitary adrenocorticotrophic hormone, ACTH Most of the features of Cushing's syndrome can be produced by the prolonged administration of ACTH, or by large doses of cortisone or hydrocortisone.

In some cases of Cushing's syndrome there may be an increased secretion of the adrenal sex steroids This would account for the hirsutism, acne and enlarged clitoris occasionally seen in women who show signs of both Cushing's syndrome and the adrenogenital syndrome (see above).

The importance of Cushing's syndrome in cardiology is that it is a cause of hypertension in young people

Symptoms.—There is a history of a recent gain in weight and the development of painful adiposity. Irritability, drowsiness and muscular weakness may develop The weakness may be so marked that in stepping up ordinary stairs the patient may have to use his hands on his legs to help lift his feet The muscle weakness may be due to actual muscular wasting, because of the action of the glycogenic corticoids In other cases, it is due to a marked potassium deficiency. Polyuria and polydipsia are frequent, due to latent or frank diabetes. Amenorrhea or impotence may occur

Signs.—The patient shows a distinctive habitus, characterized by obesity of the face, neck, and trunk, and sparing the extremities Usually there is a pad of fat over the cervicothoracic portion of the spine The eyelids and the corners of the mouth droop and when the face is viewed squarely from the front, the ears may be partially or totally concealed by the plethoric fullness of the face (moon-face) Acne of varying degrees is present. The skin is usually thin, dry and scaly and there are purplish striæ over the abdomen and thighs Hypertension is present, but it may be moderate or transient However, malignant hypertension may occur

Laboratory Tests.—There is a characteristic increase in the urinary glycogenic corticoid excretion which may reach 700 units In addition, the circulating 17-hydroxycorticosteroid level is abnormally high (The average normal level of plasma 17-hydroxycorticosteroid level is 13 + or − 6 gamma/100 cc)

The urinary 17-ketosteroid excretion may be normal or moderately increased However, if adrenal cortical hyperplasia or an adrenal cortical tumor is the cause of the syndrome, the 17-ketosteroid excretion becomes high The two conditions can be differentiated because in adrenal cortical hyperplasia, the beta fraction is only slightly increased, whereas in cases of adrenal cortical carcinoma, the beta fraction is greatly increased along with the alpha fraction

The following "cortisone test" can also be used to differentiate an adrenal cortical tumor from adrenal hyperplasia Daily 17-ketosteroid determinations are performed on twenty-four-hour urine specimens for at least two to four days before the test starts Then, 100 mg of cortisone are given intramuscularly for five days If the Cushing's syndrome is due to adrenal hyperplasia, the 17-ketosteroid level will fall significantly If the syndrome is due to a functioning adrenal tumor, the 17-ketosteroid excretion will remain unchanged

The blood shows a leucocytosis with lymphocytopenia and eosinopenia, due to the increased corticosteroid activity Polycythemia may be present

Blood chemistry determinations show a low potassium, a low chloride, a high bicarbonate and an elevated pH (hypochloremic, hypopotassemic, alkalosis) The serum sodium level may be normal or increased The fasting blood sugar level is normal, but the sugar tolerance is decreased

The urine may be alkaline, and show albumin, casts, and an increased calcium excretion Glycosuria may be present

X-Ray Examination—Osteoporosis is usually present because of increased glycogenic corticoid activity and is especially marked in the skull, spine,

pelvis and ribs Spontaneous fractures may occur. The sella turcica is normal However, the posterior clinoid process may disappear because of the osteoporosis X-ray examination of the abdomen may reveal an adrenal tumor

Course and Prognosis.—Patients may live many years, but serious and fatal complications may occur from the hypertension and diabetes.

Treatment—In an emergency, muscular weakness or paralysis can be corrected with large doses of potassium (page 717). This will not, of course, correct the other features of the syndrome.

In the past, x-ray irradiation of the pituitary and/or the adrenals has been used The most promising therapy is bilateral, subtotal removal of the adrenal glands.

All patients with Cushing's syndrome should have a careful x-ray examination of the adrenal areas Excretory urography may show downward displacement of a kidney, indicating a suprarenal tumor This can be confirmed by translumbar aortography, posterior laminograms, or even perirenal air insufflation Preoperative localization of an adrenal tumor simplifies the surgical problem because the tumor can be removed by way of the thoraco-abdominal or flank approach without the necessity of exploring both adrenals However, if no tumor is found, simultaneous bilateral exploration of the adrenals should be done.

It is difficult to estimate how much adrenal tissue should be left in the body Experience has shown that about 90 per cent should be removed.

Pre- and postoperative substitution therapy is very important in the surgical treatment of Cushing's syndrome The following is the schedule used by Cahill:

1 In preparation for the removal of a tumor with Cushing's syndrome, acute adrenal insufficiency is to be anticipated, since the contralateral adrenal is often without sufficient function to maintain life For this, ACTH is given in 25-mg doses every six hours for three or four days previous to operation and is continued for at least a week or more after removal of the tumor In addition, intramuscular cortisone acetate is given in 50-mg doses every twelve hours, with 5 Gm of sodium chloride by mouth given the day previous to operation, and 5 mg of DOCA (desoxycorticosterone acetate) is given intramuscularly twelve hours before operation On the day of operation cortisone acetate, 150 mg, and DOCA, 5 mg, is given one hour before operation During operation, the blood pressure is maintained with intravenous norepinephrine, 4 mg per L. Following operation there is a maintenance forty-eight-hour therapy of ACTH, 25 mg. every six hours, cortisone, 50 mg every six hours, DOCA, 5 mg every twenty-four hours, and sodium chloride, 3 to 5 Gm by mouth every twenty-four hours There is then a reduction of daily cortisone to 50 mg for forty-eight hours and DOCA to 1 to 5 mg every twelve hours The cortisone is then kept at a dose of 25 mg for three to four days more, depending upon the need, and it is stopped several days before the cessation of the ACTH

2 For subtotal resection of bilateral adrenal hypertrophy with Cushing's syndrome, no substitution therapy is necessary at the first sitting if the case is operated upon in two stages At the second sitting the patient is given, the day previous to operation, intramuscular cortisone acetate, 50 mg every twelve hours. Twelve hours before operation 5 Gm of oral sodium chloride and 5 mg of DOCA are given intramuscularly. On the operative day 150 mg of cortisone acetate and 5 mg of DOCA are given one hour before operation The case is then treated, as is the tumor, with the gradual reduction of cortisone and DOCA but with the maintenance of sodium chloride The duration of the maintenance dose varies in each case, most requiring administration from ten days to six weeks.

Hypofunction of the Adrenal Cortex

Addison's Disease.—Addison's disease results from a decrease or absence of desoxycorticosterone and other adrenal cortical hormones due to adrenal cortical atrophy, or to tuberculosis or cancer of the adrenal gland The cardiovascular system is involved in the marked asthenia that occurs, and injudicious replacement therapy with desoxycorticosterone may precipitate heart failure

Pathological Physiology —Because of the absence of desoxycorticosterone there is an excess excretion of sodium, chloride and water from the kidney, and a diminished excretion of potassium so that the blood sodium and chloride levels fall, and the blood potassium level rises The electrolyte disturbance and the loss of water may be so marked that severe hemoconcentration and shock may develop In addition the kidneys are unable to excrete urea and other nonprotein nitrogenous products and a form of extrarenal azotemia occurs

The absence of other cortical hormones causes a disturbance in fat and carbohydrate metabolism and hypoglycemia results The hypoglycemia may even produce central nervous symptoms such as convulsions

Pathology.—The heart merely shows brown atrophy or other minor changes However, in cases which have been treated with desoxycorticosterone, focal myocardial necrosis may occur

Symptoms.—Asthenia, fatigue and lethargy are early symptoms Gastrointestinal irritation with nausea, vomiting and occasional periods of intense diarrhea may occur, and there may be a marked loss of weight An increased desire for salty food may develop This alone is suggestive of Addison's disease Neuropsychiatric disturbances are common These may vary from dizziness and syncope to delirium and the development of severe psychosis Some of these disturbances are due to hypoglycemia

Signs.—A characteristic brown pigmentation of the skin, especially of the exposed parts, extensor surfaces and genitalia, and of the mucous membranes of the mouth may occur very early in the disease

The blood pressure is low and the heart rate normal. The systolic pressure varies from 80 mm to 100 mm , the diastolic pressure from 60 mm to 70 mm. However, if hypertension had been present before the onset of symptoms, the blood pressure may remain elevated During an Addisonian crisis the systolic pressure may fall to 60 mm or may be even unobtainable.

The heart is small, and the heart sounds feeble

Fluoroscopic and X-Ray Examination.—The cardiac silhouette is small; the more severe the disease, the smaller the heart shadow The smallness of the heart is probably due to the low circulating blood volume and the low cardiac output, because with hormone therapy the heart increases in size, and if excess desoxycorticosterone is given, generalized cardiac dilatation with pulmonary congestion may occur.

Calcification of the adrenal glands may be present if the Addison's disease is due to tuberculosis.

Electrocardiogram —In Addison's disease and in adrenal cortical insufficiency, hyperpotassemia is uniformly present However, the electrocardiogram may be normal, or rarely, the tall, peaked *T* waves of hyp-

potassemia may occur. Usually, the T waves are flat and their direction reversed, in spite of the hyperpotassemia. And when such cases are treated with desoxycorticosterone (DOCA or DCA) and the serum potassium falls, the T waves may become large and normal again, in spite of the lowering of the serum potassium. Or, as occurs in many cases, the T wave abnormalities may become more marked in spite of clinical improvement.

These observations are confusing. They can be partially explained when one realizes that in Addison's disease, there is more than one hormone involved. For example, the electrolyte-controlling, salt hormones such as desoxycorticosterone may be effected. Desoxycorticosterone therapy not only lowers the serum potassium level, but also causes a decrease in muscle potassium. This is probably the reason that changes in the T wave occur after desoxycorticosterone therapy.

In addition, the glycogenic "S" steroids such as hydrocortisone may be affected. These hormones tend to draw potassium out of the muscle cells and into the liver, thus lowering the serum potassium level and decreasing the amplitude of T.

The sex, "N" hormones, such as androsterone, may also be affected. Androsterone has an effect similar to testosterone and tends to draw potassium out of the blood and into the muscle cells, where it is probably held in a non-ionizable state.

In Addison's disease, the general secretion of the steroid hormones is low, but one or more groups of the hormones may be functioning more or less normally. Thus, if desoxycorticosterone is absent, potassium will be retained in the body, the serum potassium level will rise and potassium will tend to enter the muscle cells and produce the electrocardiographic patterns of hyperpotassemia. However, if the "N" hormones are also absent, there *will be a tendency for potassium to leave the muscle cells. The net effect* may be a decrease in intracellular potassium and flat and reversed T waves, in spite of the hyperpotassemia.

On the other hand, if the "N" hormones are functioning more or less normally, the potassium which enters the cells may be held in a non-ionizable state so that the electrocardiogram will remain normal, in spite of the hyperpotassemia. Some evidence for this assumption is the fact that in patients with Addison's disease who have a very low urinary excretion of 17-ketosteroids (which is an index of the "N" hormone production), the T waves are usually abnormal, whereas if the 17-ketosteroid excretion tends to approach normal levels, the T waves tend to be normal.

There are also other factors which may be responsible for the T wave abnormalities in Addison's disease. For example, organic heart disease may be present. In addition, if the patient receives vigorous therapy with desoxycorticosterone, the potassium content of the heart muscle can be lowered to such an extent that myocardial necrosis may result.

Laboratory Tests.—As was mentioned above, there is an increase in serum potassium, urea and non-protein nitrogen, and a decrease in serum sodium and chloride. There may be marked hypoglycemia. The excretion of 17-ketosteroids and glycogenic corticoids is low.

Circulation times and venous pressure are normal. The basal metabolic rate is decreased.

Diagnosis.—The asthenia, pigmentation of the skin and mucous membranes, low blood pressure and feeble heart action are characteristic of Addison's disease. The most reliable laboratory finding is a low serum sodium level of less than 130 mEq. per liter, (provided other causes of sodium loss are not present) along with a serum potassium level of more than 5 mEq./liter.

In doubtful cases, a low blood sodium level can be precipitated by means of the following *sodium restriction test*. The patient is hospitalized and placed on a low-sodium diet containing only 1.5 grams of sodium chloride a day. Daily weighing, frequent blood pressure readings and blood determinations are done at intervals of one to three days to check for the appearance of hemoconcentration (elevation of hematocrit, urea nitrogen, or non-protein nitrogen values), and for the development of sodium depletion.

A positive result consists of the development of mild anorexia, a fall of 2 to 3 kilograms of weight, with a 5 to 10 per cent rise in hematocrit, a 10 to 15 mg. rise in urea nitrogen, accompanied by a fall in serum sodium greater than 5 mEq./liter, and a rise in serum potassium above 5 mEq./liter. In some cases, hemoconcentration will not occur, but the serum sodium will fall. This is a positive result also.

If nausea develops, or if the patient vomits or shows signs of vascular collapse after the first twenty-four hours, blood should be drawn, the test stopped and an infusion of glucose and saline given. In other cases, the test should be continued for a week.

The Forty-eight Hour ACTH Test can also be used to diagnose Addison's disease. This test is based on the ability of ACTH to stimulate the adrenal glands. In Addison's disease, adrenal stimulation will not appear.

ACTH in doses of at least 25 mg. is given every six hours for a two-day period. The excretion of 17-ketosteroids during the second twenty-four hours of ACTH administration and the level of circulating eosinophiles are compared to values obtained prior to the ACTH administration.

Addison's disease is indicated if there is a rise of less than 3 to 4 mg. in the 17-ketosteroid excretion, associated with less than 40 to 50 per cent decrease in circulating eosinophiles. One cannot rely on a fall in eosinophile count alone, since this can occur even when adrenal cortical insufficiency is present. The test should not be performed if cortisone has been used, because the adrenal cortex is depressed for several days after cortisone treatment is stopped.

The 17-ketosteroid excretion is low in Addison's disease. In females, values are usually below 5 mg., and in males, usually below 7 mg. However, these low values are not specific for Addison's disease and can occur in a variety of acute infections and chronic conditions.

Course and Prognosis.—Although the patient with mild Addison's disease may live many years, death may occur rapidly during an Addisonian crisis. Addison's disease due to tuberculosis or cancer has a poor prognosis.

Treatment.—Specific treatment of Addison's disease consists of the use of adrenal cortical hormone preparations, the most potent of which is desoxycorticosterone acetate (DCA, DOCA), which enables the kidneys to retain sodium, chloride and water, and thus enables the blood potassium to fall to normal. However, it does not correct the disturbances in carbohydrate, fat and protein metabolism which also exist.

If excess desoxycorticosterone is given, there may be so much retention of sodium and water that generalized cardiac dilatation and heart failure with subcutaneous edema, an increased venous pressure, and pulmonary congestion may result. Marked hypertension may also develop from the desoxycorticosterone.

Desoxycorticosterone also affects the electrocardiogram It may cause the *T* waves to become smaller or may reverse the direction of *T* as the blood potassium falls However, if *RS–T* deviations or flat or reversed *T* waves are present due to the Addison's disease, the administration of desoxycorticosterone may cause the *RS–T* deviations to disappear and the *T* waves to become normal despite the fact that the blood potassium level falls The explanation for this is unknown. The average maintenance dose of desoxycorticosterone varies from 5 to 10 mg daily, given intramuscularly. The drug can also be given orally by the sublingual route. 0 1 cc. of solution (4 drops), which represents 1 mg can be given several times daily. Subcutaneous implantation of desoxycorticosterone pellets every nine to twelve months can also be used The intake of foods containing potassium should not be restricted while the drug is used, but the use of sodium chloride or foods with a high sodium content must be limited to some extent to avoid the development of pulmonary edema. A high carbohydrate diet should be used to combat hypoglycemia. In cases of Addison's disease with severe hypoglycemia, whole adrenal cortical extract may be necessary.

An aqueous suspension of desoxycorticosterone can also be used for long term treatment The average dose is 60 mg (or less, given intramuscularly every four weeks

Cortisone can also be used in the treatment of Addison's disease. It is particularly beneficial to those patients who do not respond to DOCA. The average daily dose of cortisone is from 12 5 to 25 mg , given in two divided doses Occasionally as much as 75 mg. a day are needed In addition, the patient usually requires from 3 to 4 grams of salt. This can be given in enteric coated tablets, or dissolved in plain water (I may point out that many patients with Addison's disease do well, merely with a daily dose of 10 to 15 grams of salt)

Treatment of Adrenal Crisis.—The treatment consists of large quantities of fluid and salt to combat the dehydration plus the use of DOCA, adrenal cortical extracts and cortisone Usually 2 to 4 liters of saline are needed daily with 5 mg of DOCA or 10 to 20 cc. of lipo-adrenal cortex, given in divided doses at six- or eight-hour intervals One must be careful not to overload the circulation, because pulmonary edema or right-sided heart failure can develop In addition, 50 to 100 mg of cortisone should be given orally immediately and an additional dose of 50 to 100 mg. given during the following twenty-four hours If the patient cannot tolerate oral medication, a larger initial dose of 100 to 200 mg cortisone should be given intramuscularly

Penicillin should be also used to combat any infection which may be present.

The Waterhouse-Friderichsen Syndrome.—This occurs during a bacteremia, usually a meningococcemia, and shows a fulminating course, usually fatal, characterized by shock, vomiting, cyanosis, and a rapidly spread-

ing purpuric eruption It is due to acute adrenal cortical insufficiency as a result of bilateral hemorrhages into the adrenal glands

Treatment includes saline infusions to combat the shock, antibiotics to combat the bacteremia, and large doses of adrenal cortical extract and cortisone (see above).

DISEASES OF THE ADRENAL MEDULLA

Pheochromocytoma and Paraganglioma.—Chromaffinoma is the general term used for tumors of chromaffin (chromaphil) tissue which are capable of secreting epinephrine and/or norepinephrine. A chromaffinoma which develops in the adrenal medulla is known as a pheochromocytoma Other chromaffin tumors may arise in the organ of Zuckerkandl just above the bifurcation of the aorta, or in the abdominal or thoracic sympathetic paraganglia (paraganglioma), and even in the carotid body and the brain The tumors are usually solitary, but extra-adrenal tumors may be multiple, especially in children The tumors are usually benign, but malignancy is *almost always associated with bilateral tumors*

Pathological Physiology—Most pheochromocytomas (chromaffinomas) are capable of secreting excessive amounts of epinephrine and/or norepinephrine, although those in the carotid body rarely do When excessive *epinephrine* is liberated into the blood stream, it causes a marked peripheral vasodilation, but it raises the cardiac output so much that systolic hypertension results In addition, the epinephrine increases the basal metabolism, *mobilizes glycogen in the liver and converts it to glucose, thus producing* a hyperglycemia and glycosuria *Norepinephrine*, on the other hand, is essentially a vasoconstrictor. It raises both the systolic and diastolic blood pressures, but its effect on metabolism and blood sugar is minimal

Usually the activity of the tumor is intermittent and paroxysmal However, persistent overactivity of the chromaffin cells results in the typical and pathological picture of chronic essential hypertension

Pathology—Histologically the functioning tumor cells can be identified by their affinity for chromates which react with the epinephrine in the cells to produce fine brown granules scattered throughout the cytoplasm. The *chromaffin cells are large and polyhedral and contain vacuoles, an eccentric* nucleus and characteristic inclusion bodies Ganglion cells may also be present in the tumor

Neurofibromatosis is commonly found in association with a pheochromocytoma

Symptoms and Signs.—In a typical case, the patient, whose blood pressure has been normal, develops a marked rise in systolic pressure to even 300 mm or more, with usually a *proportionate rise in diastolic pressure* He suddenly experiences marked palpitation due to tachycardia, severe pounding headache, pallor, especially of the face, numbness, tingling and coldness of the feet and hands, sometimes nausea and vomiting, and epigastric pain or a sense of *constriction radiating* into the precordial region There is great anxiety and sometimes a feeling of impending doom The end of the attack is accompanied by excess sweating The attack may last a few

minutes or several hours, and may occur as often as several times a day to once a month or less. During the intervening periods, the patient is usually symptomless. Other cases of chromaffinoma show a persistent hypertension with or without paroxysmal rises.

During the attack, acute pulmonary edema may also occur as well as cardiac arrhythmias, such as auricular fibrillation, premature beats or *a–v* dissociation. Electrocardiographic signs of ventricular strain or hypopotassemia may appear.

Attacks of unusual severity and duration, lasting eight to twelve or more hours may result in peripheral vascular collapse, which is similar to the epinephrine shock which can be produced in experimental animals by intravenous injection of large doses of epinephrine. Peripheral pulses and blood pressure may be unobtainable due to the extreme vasoconstriction. The skin temperature falls sharply, but the rectal temperature is elevated.

There is some evidence that when the tumor is secreting norepinephrine predominantly, the clinical picture simulates essential hypertension with negligible metabolic disturbances. Whereas, if the tumor is secreting mostly epinephrine, hypertension occurs along with an increased metabolism, hyperglycemia and tachycardia However, it has been found that patients with tumors containing large quantities of epinephrine may at times show a clinical picture indistinguishable from essential hypertension with a normal heart rate, absence of hyperglycemia, a normal metabolic rate and a negative or equivocal response to benzodioxane (see below).

Laboratory Tests.—During the attack there is an increased basal metabolic rate which may rise to +60 or higher Hyperglycemia and glycosuria may also appear and persist.

Diagnosis.—The symptoms and signs of chromaffinoma may simulate attacks of hyperthyroidism, acute anxiety states, neurocirculatory asthenia, essential hypertension with paroxysmal rises in blood pressure, diabetes mellitus, even angina pectoris or myocardial infarction.

Diagnosis can be made in one of several ways:

1 By demonstrating pressor substances in the blood during an attack. This is a difficult technical procedure

2 *Tests Which Inhibit Excessive Epinephrine and/or Norepinephrine*.—During an attack, or in a patient with persistent hypertension, the excessive epinephrine and/or norepinephrine in the blood can be inhibited by adrenolytic drugs such as benodaine (piperidylmethyl benzodioxane, 933 F), regitine, or dibenamine If one of these drugs is injected intravenously, a prompt but transient fall in blood pressure occurs as the epinephrine or norepinephrine is inhibited This is called a positive reaction It indicates the presence of a pheochromocytoma. In patients with hypertension due to other causes, the drugs may produce no change in blood pressure, a minimal fall, or even a rise. It indicates that a pheochromocytoma is absent

Either regitine or benodaine can be used with safety to inhibit the action of epinephrine or norepinephrine Regitine should be tried first as a *screening test*

With either of these drugs, the following directions are important:

1. The patient's blood pressure should be stabilized at a level of 150/110 mm. Hg. or higher, while lying. If the pressure is lower, a false negative reaction may occur

2. The patient should have no sedation or narcotics for twenty-four hours prior to the test, to avoid a false negative reaction

3. The test should not be done on a patient in uremia, which gives a false positive reaction

4 Thiocyanates should not be given for four to six days prior to the test

The Regitine Test —The test is first done intramuscularly If a positive result is obtained, the test is repeated (on another day) intravenously

Intramuscular Regitine Test —Inject 5 mg of regitine, dissolved in 1 cc sterile distilled water, intramuscularly, with the patient lying

Record the blood pressure five minutes after the injection and at five-minute intervals for the next thirty to forty-five minutes

A positive result is a drop in the systolic blood pressure of more than 35 mm Hg and a drop in the diastolic pressure of more than 25 mm within twenty minutes following the intramuscular injection This is highly suggestive of pheochromocytoma The maximal hypotension persists for approximately thirty minutes

A negative result the blood pressure remains unchanged, or slightly or moderately elevated (8 to 10 mg) or is slightly reduced (less than 35 mm. systolic, and 25 mm diastolic), following the injection

Tachycardia is the only side effect of intramuscular regitine

Intravenous Regitine Test —This is used to confirm a positive intramuscular test (However, it can be used as an initial test)

Basal blood pressure is determined, the patient resting in a supine position until the pressure is stabilized This may take twenty minutes or more The blood pressure rise following the introduction of the needle is allowed to subside to within 3 or 4 mm Hg of the basal level before injecting the regitine The drug is then injected rapidly, in a dose of 5 mg Higher doses may give a false positive result Following the administration of the drug, the blood pressure is recorded every thirty seconds for five minutes, and thereafter every minute for fifteen minutes

A positive result consists in a fall of systolic pressure exceeding 35 mm. Hg and a fall in diastolic pressure exceeding 25 mm The maximal depressor effect appears within two minutes and usually lasts about ten to fifteen minutes However, the pressure may begin to rise in about two and a half minutes

A negative result consists of. no change in blood pressure, a slight or moderate rise in blood pressure (8 to 10 mm Hg), or a slight reduction in blood pressure (less than 35 mm Hg systolic and 25 mm Hg diastolic)

A *false positive result* can occur in patients with uremia and in those who have received sedatives prior to the test Occasionally, a false positive occurs for unknown reasons in the absence of a pheochromocytoma

A *false negative result* is rare. However, it may occur if the tumor is not discharging sufficient epinephrine or norepinephrine to elevate or sustain an elevation of blood pressure at the time of the injection

Side reactions are infrequent and consist of tachycardia, weakness, dizziness or flushing These disappear spontaneously

If a positive result occurs with regitine, a benodaine test should be performed next

The Benodaine Test.—The patient should be lying in a quiet room for fifteen minutes, or until the blood pressure has become stabilized. The pressure is then recorded at intervals of thirty seconds or one minute, for a period of five minutes. An intravenous infusion of 5 per cent glucose in distilled water is then started, and repeated determinations of the blood pressure are made until the pressor effect of the needle puncture subsides Then, benodaine is injected over a two-minute period through a 3-way stop-cock attached to the intravenous infusion.

For adults, a dose of 0 25 mg. per kilogram of body weight (or 1 mg. per ten pounds of body weight), is recommended. The maximum dose should not exceed 20 mg.

A *positive result* consists of a 30 mm or more drop in both systolic and diastolic blood pressures. The pressure begins to drop *promptly after the* injection The maximal fall occurs within one to four minutes after the start, and the pressure returns to the preinjection level in about fifteen minutes, in most instances.

False positive results may occur, especially in uremia, and in patients who have been heavily sedated. Occasionally, a false negative result occurs. In such a case, the tumor was probably not secreting epinephrine or norepinephrine at the time of the test

Side Effects of Benodaine —Side reactions, such as tachycardia, flushing, nervousness, cold and clammy hands, headache, substernal distress, may occur within a minute or two after injection They usually disappear in a few minutes Rarely, a marked transient rise in blood pressure occurs in hypertensive patients who do not have a chromaffin tumor.

A marked hypertensive reaction to benodaine can be controlled by an intravenous injection of 1 cc. of Hydergine (Sandoz). This is a mixture of the ergot alkaloids and causes vasodilation and a drop in blood pressure

Dibenamine can be given in a dose of 7 mg. per kilogram of body weight intravenously in 300 cc of a 5 per cent glucose solution in physiological saline solution over a period of an hour to lessen the possibility of toxic reactions A positive result is also a significant drop in blood pressure.

3 *Tests Which Cause a Discharge of Epinephrine or Norepinephrine* — In patients who suffer from paroxysmal attacks and otherwise have a normal blood pressure, procedures which can cause a discharge of the pressor substances from the tumor can be used, for example, fright, massage of the tumor if possible, the cold pressor test (page 32), change of posture, carotid sinus pressure, subcutaneous epinephrine (1/1000) in a dose of 2 minims, or drugs such as histamine, mecholyl, tetraethylammonium chloride. Histamine is the most widely used

The Histamine Test.—Histamine can be used in suspected cases of pheochromocytoma in whom the resting control blood pressure preferably does not exceed 150/110 mm. Hg. If the resting blood pressure is higher, a false negative result may occur. Similarly, no sedatives or narcotics of any kind should be used for twenty-four hours prior to the test. A cold pressor test (page 32) should be done in conjunction with the histamine test to compare the pressor responses of these two procedures.

The patient should be lying in a quiet room for fifteen or more minutes to stabilize the blood pressure Then, the pressure is recorded at one-minute intervals for a period of five minutes An intravenous infusion of 5 per cent glucose in distilled water is then started and repeated determinations of the blood pressure are made until the pressor effect of the needle puncture subsides. Then, histamine in a dose of 0 025 to 0 05 mg is rapidly injected through a 3-way stop-cock to the intravenous infusion and the blood pressure is recorded every thirty seconds for the next four minutes, and at one-minute intervals for the remaining fifteen minutes

A positive result consists of a rise in systolic blood pressure of 60 mm Hg or more, and a diastolic rise of 30 mm Hg or more The rise occurs promptly within one to four minutes after the injection, and the pressure returns to the pre-injection level in five to fifteen minutes, or occasionally longer The positive histamine response should exceed the cold pressor test response

Occasionally, a false negative histamine result will occur in a patient with a pheochromocytoma Rarely, a false positive histamine result will occur

Side reactions consist of headache, nausea, marked sweating, and abdominal and precordial pain If the blood pressure rises very high, benodaine can be given intravenously in a dose of 15 to 20 mg

Tetraethylammonium bromide or chloride (etamon) can be given intravenously in a dose of 100 mg A positive result is also an elevation of blood pressure The tetraethylammonium salt is possibly safer than histamine because a dangerous elevation of blood pressure can be controlled by having the patient sit or stand Neostigmine (prostigmine) can also be given as an antidote

Mecholyl, in a subcutaneous dose of 25 mg has also recently been used A positive result consists in a sharp rise in blood pressure within two minutes after an initial fall, and the return of the pressure to normal fifteen minutes later. Side reactions, such as nausea, salivation, sweating, dyspnea, excessive lacrimation, *etc*, are usual

In these tests also, the development of a rise in blood pressure is characteristic but not pathognomonic of chromaffinoma because a rise may occur in a normal person who hyperreacts Similarly, a negative test does not rule out a chromaffinoma

4 *By Demonstrating the Presence of a Tumor*—Rarely, an abdominal tumor may be palpable X-ray examination in other cases may show a tumor within or outside the adrenal gland, displacing the kidney, or even flattening its upper pole if the tumor is within the adrenal X-ray examination after perirenal insufflation with oxygen is also valuable In rare cases, the tumor may be found within the thorax Occasionally the tumor is detected during sympathectomy for hypertension

5 By demonstrating excessive amounts of epinephrine or norepinephrine (urinary catechols) in the urine

Course and Prognosis —*During an attack the patient may die from acute pulmonary edema or from vasomotor collapse.* The clinical course of patients with persistent hypertension is similar to those with severe essential hypertension, and myocardial infarction and cerebral vascular accidents

are not uncommon Occasionally, secondary hyperthyroidism may occur Sudden death may also occur after minor trauma or a surgical operation

Treatment.—Surgical removal of the tumor or tumors results in complete cure. During the operation the surgeon must be careful not to manipulate the tumor too much lest a fatal amount of epinephrine be released. An intravenous dose of 20 mg. benodaine just before the tumor is handled will prevent this.

Regitine can also be used preoperatively. An injection of 5 mg. of regitine can be given intramuscularly or intravenously one or two hours before the operation and repeated if necessary to reduce the blood pressure toward normal. It can also be used in a 5 mg. dose intravenously to prevent a rise in blood pressure when the tumor is being manipulated.

Another procedure that can be done is to give 100 units of ACTH gel for two days, or 100 mg. hydrocortisone daily for three days preoperatively.

Postoperative shock may occur after the tumor is removed. This can be controlled by blood or plasma, or the infusion of norepinephrine (page 284) Another procedure that can be used to prevent postoperative shock is preoperative preparation with a high salt diet and desoxycorticosterone.

Spinal anesthesia should not be used because of its depressant effect on the blood pressure Within twenty-four or forty-eight hours, the patient is usually able to maintain a satisfactory blood pressure *without further* medication The operative mortality is about 10 to 15 per cent.

If the operation has to be deferred for any reason, the attacks can be averted by using regitine orally. The dose is 50 to 100 mg (1 to 2 tablets) several times a day If side reactions, such as tachycardia, orthostatic hypotension, nasal stuffiness, nausea, vomiting or diarrhea occur, the dose should be reduced

DISEASES OF THE ANTERIOR PITUITARY GLAND

Acromegaly.—Hyperfunction or tumor of the eosinophilic cells of the anterior lobe of the pituitary gland produces gigantism, if it occurs before puberty, and acromegaly, if it occurs after the epiphyses are closed Gigantism is not associated with any cardiac abnormalities However, acromegaly produces enlargement of the mandibles, the skull and all the viscera, including the heart which may be greatly *hypertrophied*, especially the left ventricle. This is usually but not necessarily associated with hypertension, and may be due in part to the increased cardiac output necessitated by the excessive growth of the body and the increased basal metabolic rate. Diabetes and arteriosclerosis may also be present, and heart failure is a common sequel of the cardiac enlargement.

Diagnosis.—A history of an increase in the size of the hands and feet, prognathism, a large tongue , headache and visual disturbances, with *x*-ray *signs of associated enlargement of the sella turcica, an* increased basal metabolic rate, excess pigmentation of the skin, glycosuria and other signs of diabetes are some of the more common findings in acromegaly. Hypertension is present in about 70 per cent of the cases.

Course and Prognosis.—A large percentage of patients with acromegaly die from congestive heart failure.

Treatment.—*X*-ray irradiation of the pituitary gland, or surgical extirpation of the tumor, if possible, will arrest the progression of the disease.

Simmonds' Disease.—Simmonds' disease results from complete loss of function of the anterior pituitary due to atrophy or destruction of the gland. As a result, signs of thyroid, adrenal and gonadal deficiency appear.

The heart undergoes brown atrophy. The electrocardiogram may show low voltage in the extremity leads and nonspecific *T* wave changes.

The clinical picture is one of extreme and progressive emaciation and may simulate Addison's disease, anorexia nervosa, or myxedema, and the differential diagnosis may be difficult because the 17-ketosteroid excretion and glycogenic corticoid excretion are low in Addison's disease and in anorexia nervosa as well as in Simmonds' disease. However, in myxedema, the 17-ketosteroid excretion is normal.

Long-term treatment with cortisone may be helpful.

DISEASES OF THE PARATHYROID GLANDS

Hyperparathyroidism, due to parathyroid tumor or parathyroid hyperplasia produces hypercalcemia and a characteristic shortening of the *Q–T* interval. The *T* waves remain normal. However, hypercalcemia is not always associated with a short *Q–T* interval, because if hypopotassemia (due to vomiting or other causes) is also present, the *Q–T* may become prolonged and the *T* waves flat, due to the hypopotassemia, and in spite of the hypercalcemia.

Hypoparathyroidism is comparatively rare and usually occurs after accidental removal of the parathyroid glands during thyroidectomy. Tetany with hypocalcemia occurs and causes a characteristic prolongation of the *Q–T* interval. Here again, hypocalcemia is not always associated with a prolonged *Q–T* interval.

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are not uncommon. Occasionally, secondary hyperthyroidism may occur. Sudden death may also occur after minor trauma or a surgical operation

Treatment.—Surgical removal of the tumor or tumors results in complete cure. During the operation the surgeon must be careful not to manipulate the tumor too much lest a fatal amount of epinephrine be released. An intravenous dose of 20 mg. benodaine just before the tumor is handled will prevent this.

Regitine can also be used preoperatively. An injection of 5 mg. of regitine can be given intramuscularly or intravenously one or two hours before the operation and repeated if necessary to reduce the blood pressure toward normal It can also be used in a 5 mg. dose intravenously to prevent a rise in blood pressure when the tumor is being manipulated.

Another procedure that can be done is to give 100 units of ACTH gel for two days, or 100 mg hydrocortisone daily for three days preoperatively.

Postoperative shock may occur after the tumor is removed This can be controlled by blood or plasma, or the infusion of norepinephrine (page 284) Another procedure that can be used to prevent postoperative shock is preoperative preparation with a high salt diet and desoxycorticosterone

Spinal anesthesia should not be used because of its depressant effect on the blood pressure Within twenty-four or forty-eight hours, the patient is usually able to maintain a satisfactory blood pressure without further medication The operative mortality is about 10 to 15 per cent

If the operation has to be deferred for any reason, the attacks can be averted by using regitine orally The dose is 50 to 100 mg (1 to 2 tablets) several times a day If side reactions, such as tachycardia, orthostatic hypotension, nasal stuffiness, nausea, vomiting or diarrhea occur, the dose should be reduced

DISEASES OF THE ANTERIOR PITUITARY GLAND

Acromegaly.—Hyperfunction or tumor of the eosinophilic cells of the anterior lobe of the pituitary gland produces gigantism, if it occurs before puberty, and acromegaly, if it occurs after the epiphyses are closed Gigantism is not associated with any cardiac abnormalities However, acromegaly produces enlargement of the mandibles, the skull and all the viscera, including the heart which may be greatly hypertrophied, especially the left ventricle. This is usually but not necessarily associated with hypertension, and may be due in part to the increased cardiac output necessitated by the excessive growth of the body and the increased basal metabolic rate. Diabetes and arteriosclerosis may also be present, and heart failure is a common sequel of the cardiac enlargement.

Diagnosis.—A history of an increase in the size of the hands and feet, prognathism, a large tongue , headache and visual disturbances, with x-ray signs of associated enlargement of the sella turcica, an increased basal metabolic rate, excess pigmentation of the skin, glycosuria and other signs of diabetes are some of the more common findings in acromegaly. Hypertension is present in about 70 per cent of the cases.

Course and Prognosis.—A large percentage of patients with *acromegaly* die from congestive heart failure.

Treatment — X-ray irradiation of the pituitary gland, or surgical extirpation of the tumor, if possible, will arrest the progression of the disease

Simmonds' Disease.—Simmonds' disease results from complete loss of function of the anterior pituitary due to atrophy or destruction of the gland As a result, signs of thyroid, adrenal and gonadal deficiency appear

The heart undergoes brown atrophy The electrocardiogram may show low voltage in the extremity leads and nonspecific *T* wave changes

The clinical picture is one of extreme and progressive emaciation and may simulate Addison's disease, anorexia nervosa, or myxedema, and the differential diagnosis may be difficult because the 17-ketosteroid excretion and glycogenic corticoid excretion are low in Addison's disease and in anorexia nervosa as well as in Simmonds' disease. However, in myxedema, the 17-ketosteroid excretion is normal

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Chapter 45

THE HEART IN NUTRITIONAL, METABOLIC AND OTHER DISEASES

BERIBERI

A DEFICIENCY of thiamine (vitamin B_1) in the diet may result in beriberi, either with predominant nervous system manifestations (dry form), or with predominant signs of heart failure (wet form), or there may be a combination of both forms

Pathology.—The cardiovascular pathology varies with the duration and the severity of the disease. There may be generalized dilatation of the heart, especially of the right ventricle Hypertrophy of the heart is usually not present unless the disease has been present a long time Pericardial effusion (hydropericardium) may be present Microscopic examination may reveal vacuolization (hydropic degeneration), or fragmentation of the muscle fibers and interstitial edema of the heart

Pathological Physiology.—Thiamine is one of the essential components of the enzyme systems concerned with the metabolism of carbohydrates. The thiamine unites with phosphorous and protein to form a diphosphothiamine protein which acts as an "activating" protein in enzymatic reactions involving the oxidation of pyruvic acid, which is a precursor of lactic acid Thus if a deficiency of thiamine occurs, pyruvic and lactic acids accumulate in the blood. The accumulation of these acids may cause marked vasodilatation of the peripheral arterioles, and a decreased peripheral resistance

The peripheral vasodilatation and the decreased peripheral resistance cause an increased cardiac output in the following way One of the factors on which the cardiac output is dependent is the venous return, because the heart can expel only as much blood as it receives Therefore, any factor such as peripheral vasodilatation which increases the venous return to the heart increases the cardiac output (assuming that the heart is more or less normal)

Along with the increased cardiac output there occurs a decrease in circulation times In addition, the oxygen consumption increases, and the basal metabolic rate rises The a–v oxygen difference decreases because the blood flow is so rapid that the tissues are able to withdraw less than usual oxygen from the capillary blood

The increase in cardiac output occurs mostly as a result of an increase in heart rate. However, the work of the heart is also increased, and if beriberi lasts long enough, hypertrophy of both the right and left ventricles may occur The increased cardiac output and the increased work of the

heart also causes cardiac dilatation and heart failure However, another factor responsible for the heart failure of beriberi is probably a direct toxic effect of the thiamine deficiency on the heart muscle.

Etiology.—The primary cause of beriberi is a diet deficient in thiamine. In the Orient, this is usually due to a restricted diet of polished rice. In this country, it is often seen in chronic alcoholics, drug addicts, and other persons who for one reason or another have subsisted on a restricted diet for several months Undernutrition itself or even starvation does not necessarily cause beriberi (see page 714).

Most cases of beriberi in this country also show signs of other nutritional deficiencies, particularly polyneuritis.

The actual time it takes for heart failure to appear depends on the degree of the hypovitaminosis, the kind of work the patient does, and the presence of associated cardiac disease

Symptoms.—The cardiac symptoms consist of easy fatigability, dyspnea on exertion and palpitation. Neurological symptoms such as muscular weakness, especially heaviness in the legs, soreness of the muscles and paresthesias may also be present.

Signs.—The peripheral vasodilation produces a sinus tachycardia with a rapid, jumpy, bounding pulse Capillary pulsation (page 140), a collapsing pulse (page 140), and Duroziez' sign (page 144) may also be present The skin may feel warm and flushed. The blood pressure is usually within normal, but the diastolic pressure may be low, due to the vasodilatation, and the pulse pressure wide. However, hypertension may occur in beriberi, for unknown reasons.

When right heart failure is present, there are engorged neck veins, subcutaneous edema, and enlargement of the liver. Pleural effusion, pericardial effusion (hydropericardium), ascites, and even anasarca may also be present Left heart failure with rales in the chest frequently occurs.

The Heart—On palpation the apical impulse may be weak and fluttering but this is not a constant sign The heart is enlarged on percussion A systolic pulmonary murmur, due to the rapid flow of blood through the pulmonary artery is often present. There may also be embryocardia or a diastolic gallop, due to the heart failure.

Fluoroscopic and X-Ray Examination.—Generalized enlargement of the heart is usually present. The right auricle is dilated, and a dilated superior vena cava may also be evident. Part of the general enlargement of the cardiac silhouette is due to cardiac dilatation Part may be due to pericardial effusion, just as occurs in myxedema. Long-standing cases also have ventricular hypertrophy.

On fluoroscopy, the cardiac pulsations are often forceful, but poor pulsations have also been noted. This may be due to the presence of pericardial effusion In a typical case of beriberi, the lung fields are clear, but pulmonary congestion may occur.

Electrocardiogram.—Most cases show flat or reversed T waves, characteristic of moderate hypotassemia (page 206) These changes are similar to those which occur in starvation In other cases, the $RS\text{-}T$ and T pattern of left ventricular strain may appear, even though hypertension is not present Other cases show a T wave pattern which resembles that found

in the healing stages of pericarditis (page 645) However, pericarditis does not occur in beriberi. The Q-T interval may also be prolonged This does not occur in pericarditis During recovery, peaked or tented T waves, suggestive of hyperpotassemia (page 207) may appear Sinus rhythm is present in most cases, although some patients may develop auricular fibrillation

If there is marked fluid accumulation in the body, low voltage of the QRS complexes occurs in the extremity leads

Laboratory Tests.—The venous pressure is elevated. However, arm-to-lung and arm-to-tongue circulation times are short and may remain within normal even if heart failure is present This is due to the high cardiac output A mild secondary anemia may be present, and there may be hypoproteinemia.

Other Signs.—Neurological signs of beriberi may also be present. These include tenderness of the calf muscles when they are squeezed, areas of anesthesia or hypesthesia, especially over the anterior surfaces of the legs, diminished ankle or patellar reflexes, especially on one side, impaired vibratory sensation in the lower extremities, *etc* The patient may also show the skin changes of pellagra which may be present as an independent deficiency disease Signs of scurvy may also be present.

Diagnosis.—The combination of peripheral neuritis, enlargement of the heart and right-sided heart failure with peripheral vasodilatation and sinus tachycardia is almost pathognomonic of beriberi In addition, there is a history of a thiamine deficient diet for three or more months, nonspecific T wave changes in the electrocardiogram are present, there is an absence of the usual causes of heart failure (rheumatic, hypertensive, coronary, syphilitic, or pulmonary), and after specific treatment with thiamine, clinical improvement occurs with a decrease in the heart size

Although a sinus tachycardia is usually present with signs of peripheral vasodilatation, these signs may be absent Similarly, in the advanced stages of beriberi heart disease, the patient may not respond to thiamine

The condition most likely to be confused with beriberi heart disease is hyperthyroidism However, other rare causes of heart failure such as lupus erythematosus, amyloidosis, idiopathic hypertrophy of the heart, *etc*, can simulate beriberi heart disease

Course and Prognosis.—The course and prognosis depend on the severity and the duration of the beriberi If the condition is treated in the early stages, complete recovery may occur. However, in chronic cases, when myocardial damage has developed, the beriberi may be fatal in spite of therapy with thiamine Sudden death is also not uncommon, due to acute right-sided heart failure and shock, even in the milder cases

Treatment.—Specific treatment consists of the parenteral administration of thiamine chloride in daily doses of at least 100 mg. In addition, a diet rich in thiamine and protein, including meat, liver, eggs, fresh milk, vegetables, and whole unpolished rice and whole wheat products should be freely used Vitamin concentrates, especially members of the B complex, and vitamins C and K may also be necessary

The general treatment recommended for all cases of heart failure, including oxygen, a low-sodium diet and bed rest (page 247) should be used

Mercurials and digitalis can also be given if the heart failure is severe. The patient may also require pleural or pericardial tap.

The signs of congestive heart failure usually disappear rapidly although a marked reduction in the heart size may not occur for several weeks, and the electrocardiographic abnormalities may persist for months.

OTHER VITAMIN DEFICIENCIES

Vitamin A deficiency is not associated with cardiovascular pathology. Pellagra, which is due to a deficiency of niacin (nicotinic acid), itself is not associated with any structural disturbances in the heart. However, *RS-T* deviations similar to those observed in acute pericarditis or myocardial infarction have been reported. Changes similar to those which occur in beriberi may also appear. Scurvy, which is due to a vitamin C deficiency, causes increased capillary fragility and a hemorrhagic pericardial effusion may occur. Vitamin P deficiency may also cause increased capillary fragility. Vitamin E has no effect on the cardiovascular system (and has no effect therapeutically in any kind of heart disease). Rickets, which is due to a deficiency of vitamin D, has no effect on the heart unless structural changes in the thoracic cage cause cor pulmonale. However, excess therapy *with vitamin D may cause metastatic calcification of the cardiac muscle,* the heart valves and even the media of the arteries.

UNDERNUTRITION AND STARVATION

Pathology and Pathological Physiology.—With prolonged undernutrition or starvation, the size of the heart decreases along with the decrease in body weight, and microscopic examination of the heart may reveal brown atrophy, loss of muscle striation, cloudy swelling and vacuolization of the muscle fibers.

There is a general decrease in metabolic activity, and the basal metabolic rate falls as well as the cardiac output. However, the decrease in cardiac output is relatively greater than the decrease in metabolic rate. The decreased cardiac output is effected in large part by a marked decrease in heart rate.

So-called starvation or hunger edema may occur. This is in part due to hypoproteinemia with a decreased osmotic pressure of the blood (page 128). However, recent studies have shown that edema may be present when the blood protein level is normal, and edema may be absent when the protein level is low. It is therefore possible that starvation edema may occur in a manner similar to the edema of heart failure. In other words, the low cardiac output is associated with a very low renal blood flow. This causes a retention of sodium, so that if the low-caloric diet is relatively high in sodium, retention of fluid and edema occur (page 129). As a matter of fact, edema, dyspnea, tachycardia and other signs of frank heart failure may appear rapidly if food is given abundantly in an attempt to hasten recovery.

Symptoms.—Because of poor muscle tone, there may be pooling of blood in the lower extremities and a decreased venous return on standing, so that dizziness may occur on sudden rising, or syncope on standing too long. There is a chronic feeling of being cold.

Signs.—The skin is cold and dry, and cyanosis of the nail bed due to stagnation of blood is often present. A sinus bradycardia is present, and the heart rate may fall to 40 or less. The blood pressure is low, especially the systolic pressure, so that the pulse pressure is narrow. A marked fall in blood pressure may occur as a result of marked undernutrition or semistarvation if hypertension has been previously present. Edema is often present for reasons discussed above.

Fluoroscopic and X-Ray Examination.—The cardiac silhouette shrinks greatly, but there are no other characteristic findings.

Electrocardiogram.—In addition to sinus bradycardia, the amplitude of the *T* waves becomes low. Similar changes have been noted after eating, due to a decrease in blood potassium level which occurs (page 716).

Laboratory Tests.—The venous pressure is low and may even be half the normal value. However, with the onset of heart failure, the venous pressure rises. The arm-to-tongue circulation time is prolonged, even if heart failure is not present, because of the decreased cardiac output.

Diagnosis.—The diagnosis of undernutrition is self-evident. In such cases, the presence of edema should not be considered as a sign of heart failure, unless other manifestations of failure are present.

Course and Prognosis.—A person may suffer from malnutrition and semistarvation for many years, and death often occurs from intercurrent infection.

Treatment.—A high-caloric, low-sodium diet, with vitamin supplement is necessary. The sodium content of the food should be kept low, especially at first, to prevent the occurrence of heart failure.

OBESITY

Although obesity can cause an increase in epicardial fat, and fatty infiltration between the superficial muscle fibers, it does not cause heart disease itself, and the effects of obesity on the cardiovascular system are indirect. For example, with an increased intra-abdominal fat, the diaphragm is elevated and the vital capacity reduced. In addition, the cardiac output rises greatly above normal during exercise and work, because the skeletal muscles must move a larger bodily mass. As a result, dyspnea on relatively mild exertion, or orthopnea is common even if the heart is normal, and in patients with organic heart disease, the presence of obesity can precipitate or aggravate heart failure. It has also been shown that there is a relation between obesity and hypertension.

Fluoroscopic and X-Ray Examination.—The diaphragm is high and the heart usually transverse. If there is a large triangular fat pad at the apex, the cardiac silhouette may simulate that of left ventricular enlargement.

Electrocardiogram.—The electrocardiogram is normal. A deep Q_3 and a downward T_3 have been noted, but lead *aVF* is normal.

Treatment.—A low-caloric, low-sodium diet (page 250) can be used. Benzedrine or similar substance can be used to curb the appetite, even if there is concomitant heart disease. However, in the presence of hypertension or coronary artery disease, small doses should be used. (5 to 20 mg. of benzedrine daily.)

HYPOPOTASSEMIA

Etiology – There are several factors which tend to decrease the level of serum potassium and to cause hypopotassemia:

A *Hypopotassemia Due to a Loss of Potassium from the Body.*—This can occur in at least two ways:

1 Severe vomiting or diarrhea due to any cause. The gastric secretions contain approximately ten times as much potassium as the serum, and the intestinal secretions contain approximately twice as much potassium as the serum Normally, almost all of the potassium in these secretions is reabsorbed into the blood, but when diarrhea or vomiting occurs, the consequent loss of potassium may cause severe hypopotassemia

In such cases, the actual level of the serum potassium may be misleading because if severe dehydration and hemoconcentration are present, the serum potassium values may be normal or even slightly increased, despite the abnormally low potassium content of the muscle cells. However, the electrocardiogram will show characteristic signs of hypopotassemia

Colitis, sprue, celiac disease and dysentery are some of the conditions in which hypopotassemia may occur as a result of potassium loss in the stools Prolonged vomiting due to pyloric or intestinal obstruction, diabetic acidosis, *etc*, are common conditions in which hypopotassemia occurs as a result of potassium loss in the vomitus. However, during the treatment of diabetic acidosis, the electrocardiographic abnormalities often become more marked during the course of treatment, because if large quantities of glucose and insulin are given (as they usually are) the liver will require large quantities of potassium for the conversion of glucose to glycogen (see below) and the potassium content of the muscle cells and the blood will be further depleted (This is the reason that it is advisable to check therapy in a case of diabetic acidosis with the electrocardiogram, because in many cases it will be necessary to give potassium orally or parenterally to make up the potassium deficiency.)

2 Loss of potassium through the urine Potassium is also lost from the body in cases of inanition or semi-starvation, or post-operatively, where there is also a very low intake of potassium in the food and a continued loss of potassium through the urine In such cases, marked hypopotassemia may occur. In addition, there are certain cases of chronic nephritis in which a marked loss of potassium occurs in the urine. Mercurial diuresis can also cause excretion of large quantities of potassium. The hypopotassemia produced by cortisone, ACTH, and desoxycorticosterone (DOCA or DCA) is probably also due to this mechanism, as is the hypopotassemia which occurs in Cushing's syndrome.

In all the above conditions, the blood calcium level may be normal, elevated, or lowered

B *Hypopotassemia Due to Transfer of Potassium from the Blood and Muscle Cells to the Liver* —Potassium is needed by the liver in order to convert glucose to glycogen. Thus, the ingestion of food, particularly carbohydrates, causes the secretion of insulin, which stimulates the liver to form glycogen. As a result, potassium enters the liver and its levels in the blood and in muscle cells fall A similar lowering of the blood

and muscle potassium occurs after the parenteral injection of insulin, and a similar shift of potassium from muscle and blood to the liver is probably the cause of attacks in cases of familial periodic paralysis A similar lowering of the blood potassium occurs after the injection of epinephrine and with sympathetic stimulation

The blood calcium level remains unchanged with such shifts of potassium

C. *Hypopotassemia Due to a Transfer of Potassium from the Blood into the Muscle Cells*—Some of the lowest blood potassium levels on record have been produced by the administration of large doses of testosterone However, the electrocardiogram in such cases usually remains normal The explanation for this is that when nitrogen is converted into protein, it requires potassium Therefore, a substance like testosterone, which produces a positive nitrogen balance, causes the entrance of potassium into the muscle cells One might suppose that in such cases the electrocardiogram would show the pattern of hyperpotassemia, but this does not occur The reason is probably that most of the potassium is held within the cell, bound to the protein in a non-ionizable state (Even in a normal person, much of the intracellular potassium is in a non-ionizable state)

D *Hypopotassemia Due to Other Causes*—Some other common causes of hypopotassemia are

1 Low serum potassium levels have been found in poliomyelitis and in other infections

2 Alkalosis usually occurs in association with hypopotassemia

3 Transient hypopotassemia may result from overhydration with potassium-low fluids

Clinical Picture.—There are no symptoms or signs with mild degrees of hypopotassemia However, when the hypopotassemia becomes severe, muscular weakness, drowsiness, anorexia, nausea, intestinal distention, paralytic ileus, muscular paralysis and shallow, infrequent respirations may occur Death is usually due to respiratory paralysis

If a patient is taking digitalis, the development of hypopotassemia can precipitate digitalis toxicity

Electrocardiogram.—See page 206

Treatment.—The average daily intake of the potassium ion ranges from 50 to 75 mEq This is equivalent to 3 73 to 5 6 grams of potassium chloride (One gram of potassium chloride is equivalent to 13 mEq of potassium) Therefore, if hypopotassemia is present, 100 to 150 mEq of potassium (7 46 to 11 2 grams of potassium chloride) can be given daily

It is preferable to give potassium orally, if possible The potassium can be given as potassium chloride in a 25 per cent solution, *viz*

℞

Potassium chloride	*15*
Syrup of orange	*60*

Each teaspoonful contains approximately 1 gram of potassium chloride (13 mEq of potassium)

Another palatable potassium preparation is Oral Potassium Triplex Solution (Lilly), which contains a mixture of potassium salts dissolved in

a glycerin solution. Each teaspoonful is also equivalent to approximately 13 mEq potassium.

If the patient cannot take potassium by mouth, it can be given intravenously in a solution containing 3 grams of potassium chloride (39 mEq of potassium) per liter The rate of infusion should not exceed 20 mEq. of potassium per hour. Solutions with a concentration of more than 50 mEq potassium per liter should not be used intravenously.

If dehydration and acidosis are present along with the hypopotassemia, Darrow's solution can be given intravenously. Each liter contains 35.5 mEq potassium, 121 mEq sodium, and 103.5 mEq chloride

Potassium can also be given rectally Twenty cc. of a 25 per cent solution of potassium chloride (5 grams) can be instilled into the rectum with a rubber bulb syringe Or a continuous rectal drip of 1/10 per cent potassium chloride can be given

HYPERPOTASSEMIA

Etiology.—The factors which tend to increase serum potassium levels and to produce hyperpotassemia are:

1 Increased intake of potassium salts If the renal function is normal, even large quantities of potassium may be taken with only transient electrocardiographic changes However, if renal disease is present, severe and even fatal potassium poisoning, with characteristic electrocardiographic findings, can occur.

2 Decreased urinary excretion of potassium. This occurs in uremia or renal insufficiency with acidosis, especially with oliguria or anuria (However, in some cases of uremia, the kidneys may excrete large quantities of potassium, so that hypopotassemia may result)

3 Tissue breakdown (as in crush syndrome, hemolysis of red blood cells due to transfusion reactions, *etc.*), anoxia, shock of dehydration. In some cases the serum potassium level may be high but muscle potassium low The electrocardiogram will indicate the low muscle potassium levels rather than the high serum potassium levels in such cases

4 Adrenal cortical insufficiency In Addison's disease, or in other cases of adrenal cortical insufficiency, there is a marked loss of sodium and chloride through the urine and a retention of potassium Hyperpotassemia therefore results However, it is only rarely that the electrocardiogram shows signs of hyperpotassemia, and in most cases of Addison's disease, low *T* waves or reversal of the direction of *T* occurs This is discussed further on page 697

5 Muscular exercise This is associated with a loss of potassium from the muscle cells, and as a result the serum potassium increases. After severe exercise, in a normal person, the amplitude of *T* increases This does not always occur because exercise is associated with sympathetic stimulation which tends to cause a decrease in serum potassium (page 717). Another factor which determines the *T* wave changes after exercise is the state of the heart muscle because myocardial anoxia (see page 297), or left ventricular strain (page 210) may occur Exercise may also cause a depression of the first portion of the *RS-T*, due, not to any electrolyte changes, but to the *Ta* wave of the auricles.

6 Acidosis is usually associated with hyperpotassemia, but hypopotassemia may also occur with acidosis, as in diabetic acidosis

Clinical Picture.—Vague muscular weakness is usually the first symptom of hyperpotassemia. This is followed by a loss of muscle strength and later by a complete flaccid paralysis of the extremities and to a lesser degree of the trunk, but usually sparing the muscles supplied by the cranial nerves Later, difficulty in phonation occurs with difficulty in respiration Pain sensation is usually intact, but vibratory and position sensation may be lost Numbness or paresthesias of the hands, feet, lips and tongue, may also occur This is followed later by anesthesia The patient, however, remains alert and apprehensive, even when muscle paralysis is present, and consciousness may persist until cardiac arrest and death occur

The heart rate may be slow and regular, in other cases, a rapid, irregular rate may be present (see page 208)

Electrocardiogram.—See page 207

Treatment.—The most important thing is to find out the cause of the hyperpotassemia and correct this, if possible However, the following can be done to decrease the serum potassium levels:

1 Do not give food or fluid which has a high potassium content Therefore, most fruits, fruit juices, legumes and nuts should be avoided Vegetables should be eaten after they are boiled and drained Eggs, butter, cream, and sugar can be used (Also see page 734)

2 Glucose and insulin can be given parenterally (see page 716) Twenty-five cc of a 25 per cent glucose solution can be given intravenously. Regular insulin can be given subcutaneously at the same time, in a dose of 1 unit for each 2 grams of glucose injected The glucose and insulin can be repeated at two-hour intervals, if necessary

3 Calcium gluconate, in a dose of 1 gram (10 cc. of a 10 per cent solution) can be given slowly intravenously, and repeated if necessary The calcium increases the rate at which the ventricles are beating and tends to prevent cardiac arrest

4 Salt is very valuable in cases of hyperpotassemia where the patient has been on a restricted salt intake Five to 10 grams of table salt can be given in the food, or a liter of normal saline given intravenously (This is equivalent to 9 grams of salt) Salt has also been given in a hypertonic solution, for example, 300 cc of a 3 per cent solution (9 grams)

5 Testosterone also is able to lower the blood potassium level (page 717) It can be given in an initial dose of 50 mg. intramuscularly, and repeated for four or five days in a daily dose of 25 mg.

6 An artificial kidney is helpful, if available

7 Cation exchange resins (page 268) theoretically may be helpful

8. Continuous gastric suction or lavage with saline, or continuous perfusion of the large bowel with a 5 per cent glucose in saline solution can also remove large quantities of potassium

Repeated electrocardiograms or serum potassium determinations should be used to check the therapy However, in cases of Addison's disease, the electrocardiogram cannot be used as a guide to hyperpotassemia (see page 700)

Hypocalcemia and Hypercalcemia.—See page 208.

ACIDOSIS AND ALKALOSIS

Marked changes in the *RS–T* segment and *T* wave of the electrocardiogram may occur in both acidosis and alkalosis, depending on the nature of the electrolyte disturbances present The electrocardiographic changes in diabetic acidosis have already been mentioned on page 692.

AMYLOID HEART DISEASE

Amyloidosis is a disease in which amyloid, an unusual protein-polysaccharide compound is deposited perivascularly in certain organs There are four main types of amyloidosis, although some overlapping occurs:

1 **Primary Amyloidosis.**—There is no apparent etiology. The maximal deposition of amyloid occurs in the heart, lungs, skin, mucous membranes, gastrointestinal tract, other smooth and striated muscle, and the lymph nodes The amyloid deposits stain poorly or bizarrely to the usual amyloid stains.

2 **Secondary Amyloidosis**—This is usually due to chronic infections, chronic suppuration or to neoplasms. The maximal deposition of amyloid occurs in the liver, spleen, kidneys and adrenal glands. The heart is affected only rarely The amyloid deposits stain with characteristic color formation to the usual amyloid stains

3. **Amyloidosis Associated with Multiple Myeloma.**—The heart is affected in about 10 per cent of these cases.

4 **Tumor-Forming Amyloidosis of the Subcutaneous Tissues and Mucous Membranes.**—The heart is not involved.

Pathology and Pathological Physiology.—There may be a localized or diffuse interstitial deposition of amyloid throughout the heart. The muscle fibers which are compressed may undergo atrophy. The coronary arteries may also be compressed by the amyloid masses, which may even invade and distort the heart valves Amyloid deposits may also occur on the visceral pericardium The aorta and pulmonary artery may also be involved, and the perivascular infiltration of the lungs may be so marked that pulmonary hypertension and chronic cor pulmonale may result.

The infiltration of amyloid in the heart can therefore disturb cardiac function and produce heart failure in the following ways: by causing compression and atrophy of the muscle fibers, by infiltration of the valves, causing valvular stenosis or insufficiency, by compressing the coronary arteries, producing myocardial anoxemia; and by involvement of the pulmonary vascular system producing cor pulmonale.

Symptoms and Signs.—In addition to the symptoms and signs of heart failure, the following other manifestations of amyloidosis may be present:

1. Sclerodermic, papular, nodular, or eczematous deposits of amyloid They often have a waxy appearance, and are frequently found about the eyelids or mucocutaneous junctions Infiltration of the face may produce a mask-like facies Additional nodular lesions may be found in the vagina, tongue, periarticular tissues, or skeletal muscles.

2 Generalized macroglossia with dysphonia or dysphagia.

3. Local or generalized lymphadenopathy, due to amyloid deposition in the glands.

4. Muscle and joint pains, and even disturbances in gait, if the skeletal system is involved

5. Abdominal pain from involvement of the gastrointestinal tract. Involvement of the mucous membrane of the stomach may cause ulceration and severe hematemesis.

The Heart.—No characteristic findings are present. If the valves have been invaded, murmurs may appear and resemble those of rheumatic heart disease.

Fluoroscopic and X-Ray Examination.—Generalized cardiac enlargement is present.

Electrocardiogram.—Nonspecific abnormalities of the T wave are present. Low voltage of the QRS may occur in the extremity leads if there is extensive amyloid infiltration of the heart.

Laboratory Tests.—The congo red test may be positive, but often is negative. A moderate hypochromic anemia and a moderate increase in sedimentation rate have been reported, as well as a reversal of the albumin-globulin ratio in the blood. The venous pressure is elevated and circulation times prolonged as in ordinary cases or right- and left-sided heart failure.

Diagnosis.—Amyloid heart disease should be suspected when chronic intractable heart failure occurs in the absence of the usual etiological factors. In such cases, search should be made for macroglossia or characteristic skin and mucous membrane lesions. The congo red test is characteristic only if positive. Biopsy of accessible lesions may reveal the amyloid deposits. Heart failure occurring in the course of multiple myeloma is also suggestive of amyloid heart disease.

Course and Prognosis.—Once heart failure sets in, it is relatively refractory to therapy, and the clinical course is progressively downward. However, some patients may live for years, even after the onset of symptoms.

Treatment.—There is no specific treatment for primary amyloidosis, although dessicated whole liver preparations have been used in the treatment of secondary amyloidosis. Heart failure is treated in the usual way.

PRIMARY ESSENTIAL XANTHOMATOSIS

Primary essential xanthomatosis is a hereditary disturbance of cholesterol and lipoid metabolism in which lipoid infiltration of various organs occurs. There are two main forms, with or without hypercholesterolemia. Primary essential xanthomatosis without hypercholesterolemia affects the skin, bones and central nervous system, but not the cardiovascular system.

Primary Essential Xanthomatosis With Hypercholesterolemia.—In this form of xanthomatosis, xanthomatous deposits occur in the skin, especially over the extensor joint surfaces, and under the eyelids (xanthelasma), in tendon sheaths, in the liver and spleen, in the major blood vessels and even in the heart valves. Microscopic examination of the lesions show characteristic foam cells. As a result of the xanthomatous infiltration of the coronary arteries, angina pectoris or myocardial infarction, or sudden death is common even in young adults or children.

Symptoms and Signs.—There may be no symptoms, but angina pectoris may occur if the xanthoma involves the coronary arteries. Unusual murmurs may appear when the heart valves are involved.

Diagnosis.—The yellow skin lesions and nodules over the joints and tendons, in association with hypercholesterolemia make the diagnosis easy Biopsy of the lesions reveals the characteristic foam cells.

Treatment.—A low-cholesterol, low-fat diet (page 583) should be used indefinitely Lipotropic substances (page 585) may also be valuable.

PAGET'S DISEASE

Paget's disease (osteitis deformans) causes the formation of small, multiple, arteriovenous fistulas in the affected bones This, in turn, causes an increased cardiac output, cardiac enlargement, and eventually high-output heart failure, just as a large peripheral arterio-venous fistula does (page 663) *If the Paget's disease causes marked deformity of the* thoracic spine, cor pulmonale may also develop

ANEMIA

Severe chronic anemia, regardless of its etiology, can result in cardiac dilatation, hypertrophy and severe and even fatal heart failure.

Pathological Physiology.—When the red blood count and the hemoglobin fall, the following three compensatory mechanisms appear to prevent inadequate oxygenation of the tissues:

1 Vasodilatation occurs and the cardiac output rises. Normally about 5 5 volumes per cent oxygen are given up by the capillaries to the tissues (see page 131). However, if the hemoglobin falls to 5 grams per 100 cc. blood, the arterial oxygen content falls to about 6 5 volumes per cent. In such a case, it would be extremely difficult for the tissues to absorb 5 5 volumes per cent oxygen even if the blood remained in contact with the tissues for an indefinite time, because as the oxygen diffuses from the capillaries, the oxygen tension of the capillary blood falls so low that very little hemoglobin can become dissociated, and as a result tissue anoxia occurs. With tissue anoxia, there is an accumulation of carbon dioxide, lactic acid and other acid metabolites, which cause arteriolar dilatation and a greater blood flow to the tissues This results in an increased venous return and an increased cardiac output (see page 711). The increased cardiac output is effected mostly by an increase in heart rate. However, the stroke volume also increases, and if the anemia persists for any length of time, cardiac hypertrophy may result.

2 The tissues extract proportionately more oxygen from the capillaries than normally. In cases of severe anemia, as much as 80 to 90 per cent of the available oxygen is withdrawn from the capillaries, instead of a normal volume of about 30 per cent. This tends to make the *a–v* oxygen difference greater than normal However, the initial arterial oxygen content is so low that even when a large percentage of the oxygen is removed, the *a–v* oxygen difference may be smaller than normal For example, when a normal person with an arterial oxygen saturation of 19 volumes per cent gives up 5.5 volumes per cent to the tissues, the *a–v* oxygen difference is 5 5 volumes per 100 cc. blood, and the percentage of oxygen given up is 5.5/19, or

approximately 28 per cent. However, if the arterial oxygen saturation falls to 8 volumes per cent, and the tissues remove 4 volumes per cent, the a–v oxygen difference is only 4 volumes per 100 cc blood, but the percentage of available oxygen removed is 4/8 or 50 per cent

3 Redistribution of blood occurs The blood is redistributed to organs where it is needed and the blood flow through such organs as the kidneys is sharply decreased.

All these methods of compensation may be adequate while the subject is at rest, but on exercise or exertion further compensatory changes may be impossible, and signs of congestive heart failure appear The level at which the compensatory changes become grossly inadequate is a hemoglobin content of 7 grams per 100 cc of blood (about 54 per cent hemoglobin) However, signs of circulatory embarrassment may appear even when the hemoglobin level is 8 or 9 grams per 100 cc. The heart failure which occurs is of the high output type (page 230)

Pathology — In addition to general cardiac dilatation and cardiac hypertrophy, long-standing cases of anemia may show fatty degeneration of the heart muscle in the form of yellow streaks (tigering) This, however, is not specific for anemia

Symptoms.—Weakness, palpitation and dyspnea on exertion may occur even if heart failure is not present, but these symptoms become greatly aggravated when heart failure occurs Anginal pains may also appear, especially in elderly patients with coincidental coronary artery disease

Signs —Marked pallor is present Edema may also be present, even though other objective signs of heart failure are absent The edema is probably produced in a way similar to starvation or hunger edema (page 714).

Because of the peripheral vasodilatation, a tachycardia, a collapsing pulse (page 140), *pistol shot arterial sounds (page 144), capillary pulsation* (page 140), Duroziez' sign (page 144) may be present The blood pressure tends to be low, especially the diastolic, due to the vasodilatation, and the pulse pressure wide

The Heart —The apical impulse may be displaced outside the midclavicular line It is forceful and bounding Enlargement of the heart may be found on percussion A sharp, snapping apical first sound may be present (page 157) A pulmonary systolic murmur is common due to the rapid flow of blood through the pulmonary artery A systolic apical murmur may also be present, due to functional mitral insufficiency, produced by dilatation of the heart and of the mitral valve ring The dilatation of the heart may also result in an apical diastolic murmur which simulates the murmur of mitral stenosis (page 168) A diastolic gallop, or embryocardia may also be present

Fluoroscopic and X-Ray Examination.—General dilatation of the heart may be present. The enlargement of the heart disappears as the anemia is treated and the red blood count rises.

Electrocardiogram —Sinus tachycardia is usually present Minor T wave changes may also appear The P–R interval may be prolonged However, if the anemia is severe, RS–T deviations, typical of myocardial anoxia (page 297) may develop.

Laboratory Tests.—The red blood count is often less than 3 million and may be less than 2 million The hemoglobin values show a corresponding decrease and may fall below 5 grams. The arm-to-lung and arm-to-tongue circulation times are short, due to the increased cardiac output, and may remain within normal limits even when heart failure is present. The venous pressure is normal, but rises with the onset of right-sided heart failure. The basal metabolic rate may be normal or elevated. The vital capacity is diminished

Diagnosis.—The diagnosis of heart failure and of anemia is simple. It is important, however, to recognize that anemia may be the cause of the heart failure, even in the absence of organic heart disease, and that if organic heart disease is also present, the anemia can precipitate or aggravate the heart failure

Course and Prognosis.—Long-continued anemia may result not only in heart failure but in marked hypertrophy of the right and left ventricles

Treatment.—Both the heart failure and the anemia should be treated. The heart failure is treated according to conventional methods (page 247). The cause of the anemia should be determined and the necessary treatment started Thus, in cases of pernicious anemia, liver extract and folic acid would be used Anemia due to long-continued, low-grade hemorrhage, as from a bleeding peptic ulcer, or repeated epistaxis, requires iron, and active therapy to the source of the hemorrhage.

Transfusions may also be necessary However, not more than 250 cc of whole blood should be given at one time, and the patient should be propped up in bed to avoid the development of acute left-sided heart failure with pulmonary edema, due to the rapid increase in circulating blood volume. (The cause of heart failure following a transfusion is *not the blood* itself but the sodium chloride in the blood. A liter of blood contains more than 3 grams of salt) Instead of whole blood, packed red cells re-suspended in 5 per cent glucose in distilled water can be used.

Sickle Cell Anemia.—Sickle cell anemia can produce the clinical picture described above, but it is particularly important because it can simulate rheumatic fever.

Sickle cell anemia is a hereditary disease almost exclusively found in Negroes, and is characterized by the presence of abnormal elongated and sickle-shaped red blood cells From 6 to 10 per cent of Negroes possess the sickle trait—their red blood cells have the capacity to sickle—but most of these individuals do not develop the anemia

Pathological Physiology.—The anemia is a hemolytic anemia and is due to agglutination of the red blood cells with erythrostasis and hemolysis in the blood vessels throughout the body. Sickling is greatly accelerated by conditions that produce anoxia, so that hemolytic crises often appear during an acute infection During a hemolytic crisis, fever may occur with varied other manifestations depending on the organs in which the intravascular thromboses have occurred. Thrombosis in the splenic vessels may result in an infarct of the spleen, with intense abdominal pain, nausea and vomiting. The hemolysis may be sufficient to cause jaundice. Thrombosis of the small vessels in the bones near the large joints may produce marked arthralgia with tenderness of the joint. Ulceration of the legs, above the

ankles, is common. Thromboses in the small and medium-sized pulmonary arterioles may lead eventually to cor pulmonale.

Symptoms and Signs.—These are similar to those found in any severe anemia (page 723) The presence of an apical diastolic murmur and a snapping first sound at the apex has often been mistaken for the murmur of rheumatic mitral stenosis

X-Ray Examination.—Enlargement of the heart will occur with heart failure The long bones show prominent trabeculations in the cortex, a bizarre architecture and periosteal elevations The skull may show radial striations that produce a "hair-on-end" appearance

Electrocardiogram—The *P-R* interval may be prolonged and nonspecific *RS-T* and *T* changes may appear.

Laboratory Tests.—The sedimentation rate is normal despite the anemia and the intravascular thromboses The white blood count may be high. There is an increase in serum bilirubin and in urine urobilinogen, due to the hemolytic anemia present The anemia itself is often severe, and the red blood count may fall to between 1 and 2 million

Diagnosis—Sickle cell anemia should always be suspected in a young colored person who shows signs of heart disease The presence of a very severe anemia, sickle cells in the peripheral blood, scars over the tibia and increased blood bilirubin are characteristic of the disease

If simple inspection of an ordinary blood smear does not reveal sickling, it can be demonstrated in the following ways Since the number of sickled cells increases greatly with anoxemia, the finger should be pricked after its circulation has been occluded with a rubber band for several minutes, or if a drop of blood is sealed between a cover slip and a slide, the decrease in oxygen tension due to the oxidative processes in the red blood cells leads to an increase in sickling in a few minutes This is in contrast to what happens when the sickling trait without anemia is present In such cases, the sickling does not appear until twelve or more hours have elapsed In addition, anemia and signs of active blood regeneration are absent.

One should remember that sickle cell anemia and rheumatic heart disease can coexist In such cases, the rheumatic heart disease can be suspected if *x*-ray examination shows marked enlargement of the left auricle, or if the electrocardiogram shows large, wide and notched *P* waves indicative of auricular hypertrophy, or signs of right ventricular hypertrophy, or if auricular fibrillation or flutter is present

Course and Prognosis.—Death may occur during an acute hemolytic crisis, or from intercurrent infection, or heart failure However, the disease is often chronic and the hemolytic attacks may become less frequent, so that a spontaneous "cure" may occur, even though the sickling trait remains

Hemochromatosis may also develop and cause further myocardial impairment (page 693).

Treatment.—There is no specific treatment for sickle cell anemia Multiple transfusions may be required. However, the precautions described on page 724 must be followed

POLYCYTHEMIA

Polycythemia is characterized by an abnormal increase in the red blood cell count It may be primary or secondary. Either form may cause serious cardiovascular disturbances.

Primary Polycythemia (*Polycythemia Vera or Rubra, Erythremia*).—The etiology of primary polycythemia is unknown.

Pathological Physiology.—Because of the marked increase in the red blood count, the viscosity of the blood is increased, and marked slowing of the blood flow occurs. As a result of stagnation of the blood, intravascular arterial and venous thromboses may occur in the various organs of the body and in the peripheral vessels; and coronary artery thrombosis with myocardial infarction, or cerebral thrombosis with hemiplegia or monoplegia, is not at all uncommon. These thrombotic episodes usually occur when the red blood count is 7 million or more.

The blood volume is greatly increased. This is due to the increased red cell count and not to an increase in plasma volume, such as occurs in congestive heart failure. This cardiac output does not increase and ventricular hypertrophy does not occur.

Symptoms.—Because of the sluggish blood flow, *headaches, vertigo*, visual disturbances and paresthesias may occur. Anginal symptoms may also develop after thrombosis of one of the coronary arteries.

Signs.—There is plethora of the face and conjunctiva, and the tongue is thickly coated and fissured. The hands and feet are red. There may be a *cyanotic tint to the skin because of stagnation of blood in the peripheral* vessels. Splenomegaly and hepatomegaly are present in from 75 to 90 per cent of the cases.

Ophthalmoscopic Examination.—See page 147.

Laboratory Tests.—The red blood count is 6 million or more, and may exceed 12 million. The hemoglobin is also increased but often not proportionately so that the color index may be low. In addition, there is a leucocytosis, with an increase in polymorphonuclear cells and an increase in platelets. The hematocrit reading is also increased above the normal value of 45 per cent. Normoblasts may appear in the peripheral blood, and the bone marrow shows red blood cell and megakaryocyte hyperplasia.

The circulation time is prolonged, but may be normal. The venous pressure is normal. The basal metabolic rate is increased because of the increased blood formation.

Diagnosis.—The finding of a plethoric countenance, a red blood count above 6 million with an increased hemoglobin and an increased hematocrit reading, with or without splenomegaly and the absence of acquired or congenital heart disease of the cyanotic type is characteristic of primary polycythemia.

Course and Prognosis.—The condition is a chronic one, and death often occurs as a result of some vascular thrombosis. Profuse hemorrhage may occur after minor trauma.

Treatment.—There is no cure for primary polycythemia, but several methods of decreasing the red blood count have been advocated:

1. Multiple phlebotomies, 500 cc. being removed weekly for two or three weeks can be done. The phlebotomy can then be repeated as necessary. In addition, an iron-deficient diet can be used, avoiding iron-containing foods, such as *red meat, liver, eggs, rye bread and brown cereals*. The value of such a diet, however, is controversial.

2. Phenylhydrazine hydrochloride, or acetylphenylhydrazine, which is less toxic, is seldom used now.

3 Radioactive phosphorus Polycythemia vera can be treated successfully by means of radioactive phosphorus (P^{32}) It can be given intravenously or orally The average intravenous dose is 3 5 to 4 mc The average oral dose is 5 to 6 mc If the red blood cell count does not decrease in a few weeks, more radioactive phosphorus can be given

X-ray therapy to the spleen or bone marrow, or as a general spray has also been used

Secondary Polycythemia —Secondary polycythemia occurs as a compensatory mechanism in cardiac conditions with chronic anoxemia and cyanosis, such as cyanotic congenital lesions, chronic cor pulmonale, and even cases of rheumatic heart disease with chronic heart failure

Symptoms and Signs.—The clinical picture of secondary polycythemia is similar to that of primary polycythemia, except that hepatosplenomegaly does not occur. In addition, the symptoms and signs of the primary cardiac disease are present

Diagnosis —The differentiation of secondary from primary polycythemia may be difficult However, in secondary polycythemia, there is evidence of chronic pulmonary disease or cyanotic heart disease (either acquired or congenital) or of other factors responsible for anoxia In addition, the arterial oxygen saturation in secondary polycythemia is below 90 per cent, whereas in primary polycythemia, the oxygen saturation is above this value. Splenomegaly is absent in secondary polycythemia unless nonhematological factors have produced it Finally, immature red or white blood cells most often occur in the peripheral blood in cases of primary polycythemia

Course and Prognosis —Thrombotic complications are not too frequent until the red blood count rises to 7 or more million cells Cerebral thrombosis is a common complication

Treatment —There is no specific treatment for secondary polycythemia It will abate and may disappear if the cardiac lesion causing the chronic anoxemia is relieved, as after the Blalock-Taussig operation (page 394)

Prophylactic therapy may be necessary if the red blood count is very high because of the tendency to thrombosis (see page 393)

NEUROLOGICAL DISEASES

Very characteristic electrocardiographic changes occur during attacks of familial periodic paralysis (see below), and cardiac involvement has been noted in cases of myotonia atrophica, progressive muscular dystrophy, Friedreich's ataxia, gargoylism, and in other neurological diseases of obscure origin

Familial Periodic Paralysis.—This is characterized by recurrent attacks of weakness of all four extremities, associated with a low level of serum potassium Spontaneous attacks usually occur at night, but attacks can be precipitated by the ingestion of large quantities of glucose or carbohydrate, or by injection of insulin or epinephrine, all of which lower the blood potassium The electrocardiographic changes which appear are due to the hypopotassemia and consist of slight *RS-T* deviations and widening, flattening or reversal of the *T* waves and a prolongation of the *Q-T* interval

The electrocardiographic changes return to normal as soon as an attack is over

Myotonia Atrophica.—This is a familial disease of muscle. It usually begins in the third decade of life and is characterized by weakness and wasting of muscles especially of the face, forearm and hand, and the thigh. In addition, the basal metabolic rate is low and the blood cholesterol elevated The cardiovascular disturbances include coronary atherosclerosis and myocardial fibrosis, sinus bradycardia, a low blood pressure and a small pulse. A prolonged *P–R* interval, bundle branch block and nonspecific abnormalities of the *RS–T* segment and *T* wave have also been described

Progressive Muscular Dystrophy.—This is also a familial disease of muscles affecting particularly young boys. There occurs bilateral and often symmetrical atrophy of the muscles especially of the thigh, shoulder girdle and arm, but the muscles of the hands and feet are spared. Atrophic and inflamatory changes also appear in the heart muscle and may be the cause of the heart failure which is not uncommon.

Friedreich's Ataxia (*Cerebral Type*).—This is characterized by progressive ataxia beginning in the legs and then spreading to the trunk and the arms A chronic interstitial myocarditis has been described in this condition Arrhythmias may also occur

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If acute pulmonary edema develops, venesection or the treatment described on page 237 can be used. Rapid digitalization is also helpful.

The hypertension can be treated by sedatives, magnesium sulfate, either orally or parenterally (page 295), rauwolfia (page 566), veratrum viride preparations (page 566) or hydralazine (page 573).

The Heart in Acute Renal Failure.—Acute renal failure (crush syndrome, lower nephron syndrome, lower nephron nephrosis, acute tubular necrosis) was first described in 1941 by Bywaters and Beall as a result of severe crush injuries. However, it can occur in many conditions associated with prolonged shock and renal ischemia, for example: hemolytic transfusion reactions, and other conditions causing the hemolysis of erythrocytes, such as blackwater fever, toxemias of pregnancy, infections and poisons, sulfonamides, heat stroke, burns, carbon tetrachloride inhalation.

Pathology.—Characteristic degeneration and necrosis occur in the lower part of the nephrons, that is, the thick portions of the loops of Henle and the distal convoluted tubules. In addition, there is edema and an inflammatory reaction in the interstitial spaces around the damaged and disintegrating tubules. Thrombosis of the adjacent veins may occur, as well as heme casts of the lower portions of the tubules, including the collecting tubules. The glomeruli, proximal tubules and the intermediate segments of the kidneys show very little abnormalities.

Clinical Picture.—*Oliguria, proteinuria, hematuria* and a decreasing urinary specific gravity usually are present within a few hours after the causative event. The oliguria or anuria usually lasts about ten to twelve days, but may persist for four weeks. During this time, the patient may die, not from renal disease, but usually from pulmonary edema or hyperpotassemia.

If the patient lives a week, cerebral complications such as *stupor*, delirium, convulsions or coma may occur. The delirium and coma are apparently due to excessive administration of sodium and water. A fever may be present the first few days. Leucocytosis and a rapidly progressive anemia are common. Hyponatremia is usually associated with hyperpotassemia.

Symptoms of hyperpotassemia (page 719) may occur at any stage. Delirium, convulsions, pulmonary edema, vomiting and diarrhea, severe epistaxis and other signs of renal insufficiency may first appear after the beginning of diuresis.

Treatment.—Many patients will recover with the following conservative treatment:

1. Fluid intake must be limited to about 1000 cc. daily, the amount lost through the lungs and by insensible perspiration.

2. A high-fat, high-caloric, high-carbohydrate, low-sodium, low-potassium, low-protein diet. A satisfactory diet is the fat and carbohydrate diet of Borst. This consists of 150 grams of sweet butter and 200 grams of sugar, a total of 2000 *calories a day*. *Pats of butter* can be made into 5 gram pills and frozen. Thirty such pills will provide 150 grams of butter, or 1200 calories. Sugar may be provided by carbohydrate containing foods (see below) or by table sugar, or glucose, which can be given intravenously in a 10 per cent solution.

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Pathology.—Characteristic degeneration and necrosis occur in the lower part of the nephrons, that is, the thick portions of the loops of Henle and the distal convoluted tubules. In addition, there is edema and an inflammatory reaction in the interstitial spaces around the damaged and disintegrating tubules. Thrombosis of the adjacent veins may occur, as well as heme casts of the lower portions of the tubules, including the collecting tubules. The glomeruli, proximal tubules and the intermediate segments of the kidneys show very little abnormalities.

Clinical Picture.—Oliguria, proteinuria, hematuria and a decreasing urinary specific gravity usually are present within a few hours after the causative event. The oliguria or anuria usually lasts about ten to twelve days, but may persist for four weeks. During this time, the patient may die, not from renal disease, but usually from pulmonary edema or hyperpotassemia.

If the patient lives a week, cerebral complications such as stupor, delirium, convulsions or coma may occur. The delirium and coma are apparently due to excessive administration of sodium and water. A fever may be present the first few days. Leucocytosis and a rapidly progressive anemia are common. Hyponatremia is usually associated with hyperpotassemia.

Symptoms of hyperpotassemia (page 719) may occur at any stage. Delirium, convulsions, pulmonary edema, vomiting and diarrhea, severe epistaxis and other signs of renal insufficiency may first appear after the beginning of diuresis.

Treatment.—Many patients will recover with the following conservative treatment:

1. Fluid intake must be limited to about 1000 cc. daily, the amount lost through the lungs and by insensible perspiration.

2. A high-fat, high-caloric, high-carbohydrate, low-sodium, low-potassium, low-protein diet. A satisfactory diet is the fat and carbohydrate diet of Borst. This consists of 150 grams of sweet butter and 200 grams of sugar, a total of 2000 calories a day. Pats of butter can be made into 5 gram pills and frozen. Thirty such pills will provide 150 grams of butter, or 1200 calories. Sugar may be provided by carbohydrate containing foods (see below) or by table sugar, or glucose, which can be given intravenously in a 10 per cent solution.

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Low-potassium foods include tapioca, cooked farina or cream of wheat, margarine, white rice, boiled and drained vegetables such as onions, asparagus, rutabagas or turnips, carrots, winter squash, corn, plain gelatin (not Jell-O).

Fruits such as huckleberries, or blueberries, canned pears, canned apple sauce, canned cranberry sauce, marmalade, or grape jam (be certain it does not contain sodium benzoate as a preservative)

The patient should be forced to eat as much as possible

3 If hyperpotassemia becomes severe, it should be treated promptly (see page 719).

4. If pulmonary edema occurs, it can be treated with venesection or the other methods described on page 237

The Heart in Chronic Kidney Disease. – When heart disease occurs in chronic renal disease, it is usually a result of long-standing hypertension, or associated atherosclerosis and coronary artery disease

The hypertension and cardiac enlargement which occur in chronic renal disease are usually less marked than in cases of essential hypertension However, the combination of the kidney disease and the hypertension may simulate malignant hypertension The usual methods of treating the hypertension can be used However, ganglionic blocking agents such as methonium should not be used in the presence of renal insufficiency (page 573) The rice diet may be valuable However, the low-sodium content of the diet can cause a decreased renal blood flow which may precipitate uremia or hyperpotassemia

Chronic kidney disease is almost always associated with a severe, normocytic, normochromic anemia, which can precipitate or aggravate heart failure Treatment is difficult because the anemia does not respond to liver, iron or vitamin B_{12} However, the patient can be given repeated, 250 cc. transfusions of packed red blood cells, resuspended in 5 per cent glucose in distilled water The transfusion should be done with the patient propped up in bed, the feet dangling, to prevent pulmonary edema *Oral cobalt salts may also be of value*

X-ray examination of the lungs may reveal pulmonary edema with bilateral congestion of the central and lower median lung fields, so-called *azotemic edema of the lungs* (Fig 49, page 195) This, however, is a sign of left-sided heart failure and occurs in the absence of chronic renal disease

The *electrocardiogram* may show signs of left ventricular hypertrophy and strain (page 210), nonspecific *T* wave abnormalities, the *T* wave patterns of hyperpotassemia (page 207), or hypopotassemia (page 206), signs of pericarditis (page 645) due to uremia, or prolongation of the *Q–T* interval, due to hypocalcemia

Hyperpotassemia is a frequent complication if oliguria, or particularly if anuria develops However, if the patient refuses to eat, or vomits, hypopotassemia may occur Hyponatremia may also occur, as in salt-losing nephritis

When *uremia* develops, a sterile pericarditis may appear This is usually fibrinous or serofibrinous, but a hemorrhagic effusion may also occur In most cases, it is symptomless. However, signs of acute pericarditis (page 644) may develop Uremic pericarditis is often a terminal event How-

ever, the patient may live for many weeks, and in some cases, may recover, even at this stage.

Treatment similar to that described for acute renal failure, often is very helpful, in uremia. However, it is not necessary to limit the fluid intake.

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Chapter 47

TUMORS OF THE HEART

TUMORS of the heart constitute a comparatively rare type of cardiac disorder and are mostly of academic interest However, cardiac tumors may simulate other forms of heart disease, and solitary pericardial tumors or pedunculated tumors of the auricles are amenable to surgical therapy

Classification.—There is no completely satisfactory classification of tumors of the heart, but the more common tumors can be classified in the following way:

1. Primary Tumors of the Heart —These may be benign or malignant.
   A. Endocardial Tumors (Myxoma—page 737, polypoid fibroma, various types of sarcoma, *etc*).
   B Myocardial Tumors (Rhabdomyoma—page 402, fibroma, lipoma, leiomyoma, rarely sarcoma, *etc*)
   C. Pericardial Tumors (lipoma, fibroma, angioma, teratoma, various types of sarcoma, *etc*)
2. Secondary (Metastatic) Tumors —These are always malignant.

PRIMARY TUMORS OF THE HEART

The most common primary tumors of the heart are myxoma, rhabdomyoma and sarcoma. Myxoma is described separately below Rhabdomyoma is described on page 402. The clinical picture of other cardiac tumors (primary and secondary) is described on page 738.

Myxoma.—A myxoma arises in the endothelium, especially of the left auricle, near the rim of the fossa ovalis. However, myxomata may also occur in the right auricle or the ventricles The tumor may be globular but is usually pedunculated, and may attain a diameter of 5 cm or more. On microscopic examination it is characterized by spindle-shaped cells, and acini composed of large polyhedral cells, embedded in a mucoid substance which may become hemorrhagic. There has been some question as to whether a myxoma is a true tumor or a thrombus which has become organized Most pathologists believe that it is a tumor

When the myxoma arises in the left auricle and is pedunculated, it may partially or completely occlude the mitral valve orifice, and produce the clinical picture of mitral stenosis, including an apical mid-diastolic murmur, enlargement of the left auricle and auricular fibrillation. The clinical picture of a ball-valve thrombus (page 528) may also be present.

Differentiation of a pedunculated myxoma of the left auricle from mitral stenosis may be very difficult. However, with a pedunculated tumor (whether it be a myxoma, a fibroma or even a sarcoma), the murmurs may change greatly with changes of posture, the cardiac silhouette on x-ray

examination may show an abnormal bulge, and if heart failure occurs, it is very refractory to therapy.

A myxoma can be surgically removed.

SECONDARY (METASTATIC) TUMORS OF THE HEART

Metastases to the heart are mostly carcinomatous, but sarcomata may also metastasize to the heart. The most common sites of origin of the primary *neoplasm are the lungs, the breast, the thyroid or the organs of the* thorax. The primary site may also be a carcinoma of the genitourinary tract. Melanosarcoma of the skin also often metastasizes to the heart.

The metastatic lesions usually involve the myocardium and pericardium, but rarely invade the endocardium or the valves. Carcinomatous emboli to the coronary arteries may also occur. Hodgkin's disease and other lymphoma may also invade the pericardium and myocardium. Leukemic infiltration of the heart occurs frequently.

THE CLINICAL PICTURE OF CARDIAC TUMORS

The signs and symptoms of cardiac tumors depend on the size and location of the tumor, and on whether the tumor is benign or malignant, and if malignant, whether it is primary, or secondary to malignancy elsewhere in the body.

Many cardiac tumors are symptomless and are discovered accidentally at autopsy. Occasionally, a fragment of a primary cardiac tumor may embolize and occlude a peripheral artery. Tumors of the left auricle may produce the clinical picture of mitral stenosis or of a ball-valve thrombus in the left auricle, as was described for myxoma. Tumors in the right auricle may simulate tricuspid stenosis, or may compress or invade the superior or inferior vena cava, producing the superior vena caval syndrome (page 672), or the inferior vena caval syndrome (page 675). Neoplastic involvement of the valves may produce unusual murmurs.

When the tumor spreads through the myocardium, congestive failure may occur suddenly and often without apparent cause, and is peculiarly refractory to therapy.

Involvement of the pericardium by malignant tumors may produce a hemorrhagic pericarditis with effusion, or even the clinical picture of constrictive pericarditis, because pericardial sarcomata often grow rapidly, compressing the heart, and causing the parietal and visceral pericardium to adhere together.

In patients with metastatic invasion of the heart, signs of cardiac involvement are usually obscured by the clinical manifestations of the primary malignancy and are often overlooked until some sudden episode occurs, such as the development of pericardial tamponade, or pericardial effusion, often hemorrhagic. In addition, non-cardiac tumors may compress the azygos veins, or invade the pleura causing pleural effusion, and the superior or inferior vena cava may be invaded producing signs which simulate pericardial tamponade or right-sided heart failure. In addition, carcinomatous lymphangitis of the lung may produce cor pulmonale by causing pulmonary hypertension (page 635).

Extension of the tumor to the base of the interventricular septum may injure the conduction system and result in incomplete or complete *a-v* block. In addition, paroxysmal auricular fibrillation, flutter or auricular tachycardia may occur, especially if the right auricle is invaded

Fluoroscopic and X-Ray Examination.—Cardiac dilatation or an abnormal shape of the heart due to bulging of tumor masses may be present Neoplastic involvement of the lungs and/or mediastinum may also be evident.

Electrocardiogram.—The tracing may be normal, or may show nonspecific *T* wave changes However, when the pericardium is involved, *RS-T* deviations typical of myocardial injury and pericarditis (page 645) may appear A tumor mass embolizing to the coronary arteries can produce the typical patterns of myocardial infarction

Diagnosis.—The diagnosis of cardiac tumors is difficult However, a tumor of the heart should be suspected under the following conditions.

1. If severe, progressive heart failure occurs without apparent cause and is *refractory to therapy*
2. If pericarditis with a bloody effusion occurs The fluid should be centrifuged and the sediment searched for pathognomonic tumor cells
3. If *a-v* block occurs without obvious cause

The development of any of these manifestations is more highly suspicious of a cardiac tumor if the patient has a malignancy elsewhere in the body. In such cases, the occurrence of paroxysmal auricular fibrillation, flutter or paroxysmal tachycardia is additional presumptive evidence of a spread of the tumor to the heart The suspicion is further strengthened if electrocardiographic signs of myocardial injury (page 211) are present

Course and Prognosis.—The course and prognosis vary with the nature of the tumor However, sudden death is not uncommon even with benign tumors, such as myxoma or rhabdomyoma

Treatment—A single, benign pericardial tumor, or a single myocardial tumor that bulges into the pericardium can be excised surgically Similarly, pedunculated auricular tumors can also be removed Treatment of other cardiac tumors is symptomatic Repeated pericardial taps may be necessary to remove accumulations of fluid, and deep *x*-ray therapy may be temporarily helpful

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Chapter 48

CARDIAC TRAUMA

MYOCARDIAL injury may occur from penetrating or nonpenetrating wounds and injuries to the chest wall or to the body

PENETRATING WOUNDS OF THE HEART

These are usually due to stab wounds, but may occur from fractured ribs, glass splinters, even foreign bodies penetrating the heart from the esophagus Bullet wounds also penetrate the heart but usually pass through the heart and cause death very quickly.

Pathology.—The penetrating wound may injure the musculature of the left or right ventricle or the interventricular septum or the auricles The aorta, the pulmonary artery, one or more of the coronary arteries, or even the cardiac valves, or the chordæ tendineæ or papillary muscles may also be severely injured Since the pericardium is injured along with the heart, a fibrinous pericarditis, or pericarditis with effusion, or a hemopericardium may develop.

Further complications may also develop For example, injury to a coronary artery may produce myocardial infarction A thrombus may form at the endocardial site of injury and may result in systemic embolization Injury to the lungs and pleura may also occur, with or without a hemothorax Communication between the injured lung and pericardium may produce a hydropneumopericardium

Symptoms and Signs.—The clinical picture of penetrating wounds of the heart varies greatly, depending on the extent of the injury Symptoms may develop immediately or after an interval of several hours or even days There may be pain in the chest, bleeding from the chest wound, shock, or signs of pericardial tamponade If the cardiac valves or papillary muscles have been torn, loud, harsh murmurs may appear along with rapid signs of heart failure (see page 744)

Fluoroscopic and X-Ray Examination.—Immediately after the accident, the heart may appear normal Serial x-ray examination, however, may show progressive enlargement of the cardiac silhouette, due to pericardial effusion Traumatic pleural effusion may also be present

Electrocardiogram.—The electrocardiographic changes that occur depend on the location and extent of the muscle injury, and consist of $RS-T$ deviations which resemble the patterns of pericarditis, which is often also present If one of the *major coronary arteries has been severed by the penetrating* injury, abnormal Q waves and $RS-T$ deviations, typical of acute myocardial infarction appear Bundle branch block or paroxysmal tachycardia or auricular fibrillation may also develop

Diagnosis.—The most useful sign in determining whether a penetrating wound of the thorax has injured the heart is the presence of abnormal *RS-T* deviations in the electrocardiogram. The presence of physical signs of pericarditis or pericardial effusion, or the development of the clinical picture of pericardial tamponade (page 644), due to hemopericardium, also indicates myocardial injury.

Course and Prognosis.—Death may be instantaneous, especially after bullet wounds of the heart, or may occur from shock, rupture of the heart, pericardial tamponade, heart failure or secondary infection. However, in the usual case of myocardial injury due to stab wounds, recovery is the rule.

Treatment.—External hemorrhage, if present, should be checked and therapy instituted for surgical shock, which is usually present. Whole blood or plasma should be used in preference to saline. Surgical exploration of the heart is often not necessary, but if signs of pericardial tamponade are present, and are not relieved by pericardial paracentesis, the heart should be exposed surgically, and the bleeding muscle sutured. It may also be necessary to ligate a bleeding coronary artery. This does not cause the severe pain usually associated with myocardial infarction due to coronary artery thrombosis. If a foreign body is found in the heart, it should be removed.

FOREIGN BODIES IN THE HEART

When myocardial injury is produced by penetrating wounds, a foreign body (bullet, shrapnel, needle, *etc.*) may lodge in the pericardium, the heart muscle, or in one of the cardiac chambers. Foreign bodies may also penetrate and lodge within the aorta or pulmonary artery. In rare instances, a foreign body, such as a needle, may enter one of the peripheral veins and be carried to the heart by way of the vena cava.

A small foreign body in the pericardium may remain for years without causing any cardiovascular disturbances. However, recurrent pericardial effusion may occur, or a pericardial abscess may develop around the foreign body, or constrictive pericarditis may eventually occur. Foreign bodies in the myocardium may result in necrosis of the muscle wall with rupture of the heart. A foreign body in one of the cavities of the heart may produce intracardiac thrombosis with subsequent embolization, or bacterial endocarditis, or the foreign body itself may embolize to one of the peripheral arteries, if it has been in the left ventricle. Precordial pain may also result from the presence of the foreign body, and in some cases, a severe cardiac neurosis may result.

Diagnosis.—The diagnosis is usually obvious on fluoroscopic and *x*-ray examination. A foreign body in the myocardium can be seen to pulsate with each heart beat. The electrocardiogram may be normal or may show signs of myocardial injury, depending on the length of time the foreign body has been present.

Treatment.—When a foreign body is observed immediately after the injury, it should be removed. When a foreign body in the pericardium or myocardium is found long after the injury and is asymptomatic, it need not be removed, unless it appears sharp and likely to perforate the heart muscle. Foreign bodies within the cavities of the heart should be removed, even if discovered late.

NONPENETRATING CARDIAC TRAUMA

Common causes of nonpenetrating cardiac trauma are automobile accidents where the steering wheel compresses the driver's chest, or direct blows to the chest wall by balls, bats or fists; or kicks by horses or other animals Blast accidents, falls from a height, or other accidents which produce a sudden forceful increase in intra-abdominal pressure can also produce myocardial injury. It is not necessary for either external signs of injury or for broken ribs to be present

Pathology.—Rupture of the auricles, the ventricles, the great vessels, the heart valves, the chordæ tendineæ or the papillary muscles may occur The myocardium usually shows hemorrhage which may be extensive and which may result in necrosis of muscle with later replacement by scar tissue, just as occurs in coronary artery disease and myocardial infarction. Pericarditis with effusion, and even rupture of the pericardium may occur with strangulation of the heart by the torn pericardium

Symptoms and Signs.—Severe and even fatal myocardial injury may be *present as a result of nonpenetrating cardiac trauma even though physical* examination may reveal no signs of external injury There may not even be a fractured rib

Precordial pain may develop, or palpitation due to the development of arrhythmias, such as sinus tachycardia, auricular fibrillation or auricular flutter, or auricular or ventricular premature contractions However, incomplete or complete *a–v* block may occur, possibly as a result of hemorrhage into the interventricular septum in the region of the *a–v* node

Signs of shock or of pericardial tamponade may also appear, and if rupture of the interventricular septum or chordæ tendineæ or papillary muscles occurs, unusual murmurs may appear and the patient may develop severe right-sided heart failure (see page 242)

Fluoroscopic and X-Ray Examination—No characteristic findings are present However, pericardial effusion will cause progressive enlargement of the cardiac silhouette

Electrocardiogram.—*RS–T* deviations, typical of pericarditis may occur However, if there is massive hemorrhage within the myocardium, electrocardiographic changes similar to those of myocardial infarction may appear If the injury is minimal, nonspecific *T* wave changes may appear

Course and Prognosis—Instantaneous death may occur, even though autopsy may show minimal cardiac injury In such cases, death was probably due to cardiac standstill resulting from vagovagal reflexes. In other cases, death may occur from rupture of the heart or pericardial tamponade within a few minutes or hours However, it may take several weeks or longer until the hemorrhagic heart muscle ruptures Death from heart failure usually follows rupture of a valve or papillary muscle When the myocardial injury is minimal, full recovery is the rule. The arrhythmias usually disappear although traumatic *a–v* block may persist.

Diagnosis—Every person who suffers even slight injury to his chest wall, or compression of his abdomen should receive an electrocardiogram as well as an *x*-ray examination in an attempt to find signs of nonpenetrating cardiac trauma The development of unusual murmurs, or arrhythmias im-

mediately after an accident in a person previously well is also suggestive of cardiac trauma However, one should remember that paroxysmal auricular fibrillation or flutter or premature contractions may occur spontaneously, or after accidents in which the heart could not possibly have been injured

Treatment.—Shock or pericardial tamponade are treated in the usual way However, if pericardial tamponade returns after pericardial paracentesis, it may be advisable to expose the heart surgically and suture the bleeding areas.

Patients with minimal or no symptoms but with electrocardiographic signs of myocardial injury should be put to bed for two weeks and placed on a low-sodium diet to allow the injured muscle fibers time to heal. However, every attempt should be made to prevent the patient from developing a cardiac neurosis.

RUPTURE OF THE CARDIAC VALVES, CHORDÆ TENDINEÆ, OR PAPILLARY MUSCLES

Rupture of one or more valves, chordæ, or papillary muscles may occur not only as a result of trauma, but from bacterial endocarditis, severe exertion, or even spontaneously. The valve may or may not have been normal previously. Myocardial infarction, syphilis or tuberculosis of the heart may also cause rupture of a papillary muscle. The phase of the cardiac cycle that the heart is in at the time of the accident determines which valve is injured because rupture of the valve occurs when it is closed and therefore stretched Thus, the mitral or tricuspid valve will be injured during systole, the aortic or pulmonary valve during diastole It is, however, rare for the pulmonary or tricuspid valve to be ruptured.

When a valve ruptures or a papillary muscle or even a chorda tendinea tears, the patient may actually feel a tearing sensation in his chest and may go into shock and die If he lives, heart failure occurs rapidly after rupture of a valve or papillary muscle, and the patient usually dies in a short time, but occasionally he may live for several months. After rupture of a chorda tendinea, no signs of heart failure may appear for several months.

When the mitral valve ruptures or one of its chordæ or papillary muscles tears, a very characteristic, loud, coarse, often musical systolic murmur appears immediately, most marked along the lower left sternal border, and the apex. A diastolic murmur may also develop, as well as auricular fibrillation or other arrhythmias. The systolic murmur occurs because the injured valve balloons into the left auricle during systole, producing mitral insufficiency. The cause of the diastolic murmur is obscure. Occasionally, neither a systolic nor a diastolic murmur appears (see also page 603).

Rupture of the aortic valve or of one of its chordæ or papillary muscles produces a loud, musical, diastolic murmur with physical signs of aortic insufficiency.

Rupture of the heart is described on page 602; rupture of the interventricular septum on page 602.

THE RELATION OF PHYSICAL EFFORT TO CARDIAC INJURY

Physical effort can cause cardiac trauma For example, rupture of the cardiac valves or chordæ tendineæ or papillary muscles or even the myocardium or aorta may occur after physical effort However, rupture of these structures may also occur spontaneously It is questionable whether physical effort can cause heart failure in a normal person although severe exercise or work can cause transient enlargement of the heart normally However, strenuous physical effort can aggravate pre-existing cardiac disease and can precipitate heart failure

The question as to whether severe or unusual effort can produce myocardial infarction is often difficult to decide In most cases, the myocardial infarction is the result of chronic coronary artery disease and progressive coronary artery occlusion However, severe or unusual exertion may so tax the coronary circulation that acute myocardial anoxemia or even myocardial infarction may develop, even without closure of one of the coronary arteries. In such cases, the patient gives a history of collapsing while performing the heavy or unusual work

ELECTRIC SHOCK

Electric shocks can produce auricular or ventricular premature contractions, auricular fibrillation or auricular flutter Nonspecific abnormalities of the *T* waves have also been reported. Death resulting from electricity is due to the development of ventricular fibrillation

Electroshock therapy used for mental diseases can also result in arrhythmias The electroshock causes marked vagal stimulation, and sinus bradycardia, varying degrees of *a–v* block, sinus arrest, and even death may occur. In addition, premature contractions and paroxysmal tachycardia, auricular or ventricular, and auricular fibrillation can appear The *P* and *T* waves may become transiently taller after the electroshock The increased amplitude of the *T* wave is probably due to the release of potassium by the intense muscular activity A similar increase in the amplitude of *T* occurs after severe exertion in normal subjects

The vagal effects of the electroshock can be prevented by the intramuscular injection of atropine in a dose of from 1 3 mg ($\frac{1}{50}$ grain) to 2 mg ($\frac{1}{30}$ grain) about half an hour before the shock

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Section 5. Special Conditions Complicating Heart Disease

Chapter 49

PREGNANCY AND HEART DISEASE

THE EFFECT OF PREGNANCY ON THE NORMAL HEART

The Prenatal Period.—Until the twelfth week of pregnancy no significant cardiovascular changes occur. Then, with the establishment of the placenta, the work of the maternal heart progressively increases because of the following factors.

1. The weight of the mother increases, demanding an increased cardiac output.

2. The actively growing fetus requires a relatively great volume of blood, which is supplied by way of the placenta.

3. The numerous, large, tortuous arteries and veins of the placenta produce a condition which is similar to that of an acquired arteriovenous fistula (see page 663).

4. Another factor that burdens the cardiovascular system is an increase in the plasma and total blood volume. This begins early in pregnancy and reaches its maximum of about 45 per cent above normal one month before delivery. This increase in circulating blood volume may be related to the increased production of both estrogenic and adrenal cortical compounds which have the property of retaining sodium and water in the body.

As a result of these factors, the oxygen consumption increases about 15 to 25 per cent above normal, and the cardiac output progressively increases from the twelfth week. The increase in cardiac output is at first slow until about the twenty-fourth week. Then it increases rapidly until it reaches a maximum value of from 40 to 50 per cent above normal at the thirty-sixth week. From then on it decreases till term. The reason for this is possibly that the placental shunt is slowly obliterated in the last month of pregnancy. The increased cardiac output is achieved by both an increased stroke volume and an increased heart rate. Although pregnancy causes an increase in the work of the heart, it is doubtful whether it causes cardiac hypertrophy.

Labor.—During labor, the heart again must engage in strenuous work, and it has been calculated that work may be performed which is equivalent to climbing a seven-foot flight of stairs once every three minutes, during a labor lasting twelve hours. Furthermore, the oxygen debt incurred during a long and hard second stage may be repaid for over an hour after delivery. The changes in the pulse and respiratory rate which occur during labor reflect the same situation.

The Puerperium.—Following delivery, the various changes of pregnancy slowly and irregularly return to normal over a period of weeks or months The plasma and total blood volume fall soon after delivery, due to loss of blood and to hemoconcentration, but rise again near the end of the first week of the puerperium This may be due to mobilization of extracellular fluid accumulated during pregnancy

The venous pressure rises even to abnormal values the first twenty-four hours after delivery, probably due to the effect of the ergot or posterior pituitary preparations given after delivery.

Symptoms Referable to the Cardiovascular System during Pregnancy.—Normal pregnant women may complain of dyspnea, orthopnea, palpitation, and a form of nocturnal dyspnea that resembles paroxysmal nocturnal dyspnea (page 236), and consists of sudden dyspnea, palpitation and a sense of choking However, the chest remains clear even during the paroxysm These symptoms are not due to a diminished vital capacity, which remains unchanged during pregnancy, but are possibly due to the increased respiratory activity demanded by the increased cardiac output In addition, as the uterus enlarges, it displaces the diaphragm upward, and may make the mechanical aspects of respiration more difficult Sighing dyspnea of psychic origin is also common

Signs Referable to the Cardiovascular System during Pregnancy.—Minor variations occur in the blood pressure which falls slightly in the second trimester, and rises again in the third trimester. The diastolic pressure is often low, producing a wide pulse pressure, and even a collapsing type of pulse Capillary pulsation may also be present The maximum values of the blood pressure are within the range of 140/90. However, during labor pains, the systolic pressure may rise to 140 mm. or slightly higher, and the pulse may increase ten to twenty beats per minute.

Varicosities and edema of the lower extremities are common These are due not so much to the increased pressure in the iliac and femoral veins but to obstruction to the lymphatic return from the lower extremities by the large uterus

The Heart—The apex may be displaced outward slightly due to the elevation of the diaphragm by the uterus The first sound at the apex may be sharp and accentuated, and an apical systolic murmur may be present along with a diastolic gallop (physiological third heart sound, page 40) The pulmonary second sound is accentuated and may be reduplicated, and a pulmonary systolic murmur is very common.

Fluoroscopic and X-Ray Examination.—The pulmonary artery segment may appear accentuated This may be due to the lordotic position assumed by the patient In addition, the left cardiac border may bulge in its upper segment and resemble the silhouette of mitral stenosis. Furthermore, in the *R.A.O* position, there may be retrodisplacement of the barium-filled esophagus, suggesting an enlarged left auricle

Electrocardiogram.—No significant electrocardiographic changes occur during pregnancy A Q_3 and a downward T_3 may appear but these are due to changes in the position of the heart and do not signify myocardial disease, because lead *aVF* remains normal

Laboratory Tests.—The circulation times usually become shorter because of the increased cardiac output. The venous pressure in the arm remains within normal, although in the femoral vein, it begins to rise in the early part of the second trimester, rises rapidly between the twentieth and thirtieth weeks, and then continues to rise slowly until delivery, falling quickly afterwards. The vital capacity remains unchanged. The basal metabolic rate also usually remains unchanged because the increased oxygen consumption occurs in association with a gain in weight However, a rise of the basal metabolic rate to +25 or +30 has been reported

THE DIAGNOSIS OF HEART DISEASE IN PREGNANCY

From what has just been said, it is often extremely difficult to determine whether a pregnant woman has heart disease, if she has not been examined previously, and a diagnosis of heart disease should be made, for example, only when unequivocal signs, such as the presence of a low, rumbling, mid-diastolic apical murmur of mitral stenosis, or *x*-ray evidence of marked cardiac enlargement, or definite signs of heart failure, are present

Heart failure in a pregnant woman can be suspected if there is a sudden gain in weight not accounted for by overeating, rapidly increasing dyspnea on exertion, or progressive orthopnea, or hemoptysis In addition, moist rales appear at the lung bases, and persist after deep respiration, the vital capacity falls, the neck veins may become prominent and the venous pressure of the arm rises, pleural effusion or generalized edema may appear, and the liver may become tender and enlarged. A circulation time at the upper level of normal may be a sign of impending failure.

One should remember that peripheral edema, orthopnea, dyspnea, tachycardia and palpitation are often observed during pregnancy in women without heart disease, or in those with heart disease but without heart failure. In addition, an apical systolic murmur, a systolic pulmonary murmur, a slapping, diffuse apical impulse, a collapsing type of pulse and capillary pulsation (due to the overactive circulation), a split first or second heart sound and an accentuated third heart sound, may all occur in normal women during pregnancy

THE EFFECT OF PREGNANCY ON RHEUMATIC HEART DISEASE

Ninety per cent or more of heart disease complicated by pregnancy is rheumatic in origin Congenital cardiac lesions appear in a small per cent of patients, and hypertensive, syphilitic or coronary artery disease only rarely Subacute bacterial endocarditis is an occasional complication

If a patient with rheumatic heart disease survives her pregnancy, her duration of life will not be appreciably decreased because of the pregnancy However, the patient with rheumatic heart disease who becomes pregnant takes a risk, because heart failure and death may occur during the pregnancy or puerperium, which would not have occurred had the patient not become pregnant In addition, the fetal mortality of cardiac women who become pregnant is higher than in noncardiac parturients, especially if heart failure is present.

The risks of pregnancy in women with rheumatic heart disease are related to several factors:

1. Women who have never been in failure are good risks and usually will deliver spontaneously.

2. Women with rheumatic heart disease, regardless of how many children they have previously borne, are more apt to fail after the age of thirty, and especially thirty-five years

3. If the woman has developed heart failure in a previous pregnancy, she will almost certainly fail again during pregnancy, unless the failure was due to some unusual circumstance, such as active rheumatic fever.

4. Women with long-standing mitral stenosis, with or without auricular fibrillation, are apt to fail It is comparatively unimportant whether the mitral valve alone or the mitral and aortic valves are involved.

5 Prognosis for women with marked cardiac enlargement is also poor.

Since the increasing cardiovascular demands of pregnancy reach their maximum at the ninth lunar month, it would be expected that if heart failure does occur, it will appear before this time. In the majority of reported cases, this is so The greatest incidence of heart failure occurs in the seventh and eighth lunar months, and it is comparatively rare for heart failure to appear during the first half of pregnancy.

Heart failure can first appear during labor when the demands upon the heart are suddenly increased. It may also appear immediately postpartum or even from one to six weeks after delivery. The cause of heart failure during the puerperium is often obscure During the first week, it may be related to the transient increase in blood volume which occurs The failure which occurs later in the puerperium has been likened to beriberi heart disease

The heart failure which develops late in pregnancy, during labor or within the first twenty-four hours postpartum is apt to be severe and nearly one-quarter of all fatalities from heart failure occur during labor and the twenty-four hours following it.

CARE OF RHEUMATIC HEART DISEASE COMPLICATED BY PREGNANCY

The care of the patient with rheumatic heart disease who becomes pregnant or is desirable of becoming pregnant can be considered in the following ways.

Criteria for Determining When a Cardiac Patient Should be Advised to Avoid Pregnancy.—The presence of rheumatic heart disease itself is not an indication for avoiding pregnancy. However, the patient should be considered a poor-risk, and pregnancy should be discouraged if any of the following conditions are present:

1 If she has had cardiac decompensation in the past.
2. If she is more than thirty or thirty-five years old
3. If mitral stenosis is present.
4. If auricular fibrillation with or without evidence of embolism is present.
5. If she has had acute rheumatic fever or chorea, she should be advised against pregnancy for at least two years after the subsidence of the attack.

Criteria For Recommending Therapeutic Abortion.—This is often difficult to determine. Legally, the general indication for therapeutic abortion is the presence of a condition which, if continued, will jeopardize the life of the mother. However, there are many border-line cases, where it is impossible to predict with certainty what will happen to the cardiac if pregnancy is allowed to continue. Notwithstanding, the following general suggestions can be made:

1. If a poor-risk patient (see above) becomes pregnant, and is not in failure, interruption of the pregnancy can be advised if she is seen within the first eight to twelve weeks, because the comparatively simple procedure of dilatation and curettage can be employed

2 If a poor-risk patient becomes pregnant and develops heart failure within the first five months, interruption of pregnancy should be advised as soon as the patient becomes compensated. However, no attempt should be made to evacuate the uterus by any method while the patient is in congestive heart failure The development of acute rheumatic fever is another indication for terminating pregnancy even as late as the fifth month However, one should wait until the florid phase of the disease is past

3 If a poor-risk patient becomes pregnant and develops heart failure after the fifth month, it is generally better to treat the heart failure and attempt to carry her to term, because the strain imposed by artificial induction of labor is just as great as that of spontaneous labor. However, one occasionally sees a patient who goes into heart failure, either with or without rheumatic activity, during the later months of pregnancy, and despite all medical therapy, becomes progressively worse and dies, undelivered In such cases, one has the feeling that it might have been preferable to interrupt the pregnancy, even though the patient was in severe heart failure

4 In border-line cases, one is justified in allowing pregnancy to continue if this is the first child. Despite the advice of the physician, the patient often elects to continue the pregnancy because of religious or personal reasons, and in many cases, delivers without serious complications

Methods of Interrupting Pregnancy—The method of interrupting the pregnancy depends on the duration of gestation

Cesarean Section—The presence of heart disease is no longer considered as an indication for Cesarean section, because severe and fatal heart failure and other complications may occur after the operation The development of heart failure after a Cesarean section has been related to the fact that the placenta functions like an acquired arteriovenous fistula On page 665, it was pointed out that when an arteriovenous fistula is excised, the sudden increase in peripheral resistance is often enough to increase the work of the heart and to precipitate heart failure. This is the reason that a phlebotomy of from 500 to 1000 cc is done at or immediately after the excision of the fistula Thus, when the placenta is removed during a Cesarean section, the circulatory dynamics may be strained in a similar way The reason a similar sequence of events does not occur with spontaneous labor, is that as labor progresses the contracting uterus slowly closes the arteriovenous connections within the placenta, over a period of several hours. However, if the cardiac patient has an obstetrical indication for a Cesarean section, such as dystocia, placenta praevia, *etc.*, it can be done,

Care of the Cardiac Patient during the Prenatal Period.—Even if the woman is not in failure she should be placed on a low-sodium diet (page 248) and should not be permitted to gain more than 15 to 20 pounds in weight. Anemia, if present, should be corrected with ferrous sulfate. However, anemia may be more apparent than real because with the increased circulating blood volume, the plasma volume increases more than the red cell volume so that hemodilution occurs. She should be advised against doing heavy work, excess stair-climbing, and should rest several hours during the day

She should be examined every two weeks during the first and second trimesters of pregnancy and weekly thereafter, special search being made for early symptoms or signs of heart failure (page 751). She should be admitted to the hospital for observation a week before the expected date of delivery so that her activities can be controlled.

With the onset of heart failure, the patient should be hospitalized, put to bed and placed on a rigid low-sodium diet, mercurial diuretics and digitalis. The bowels should be kept open with mild cathartics rather than with enemas which may cause straining and prematurely induce labor.

She should be kept at bed rest until the signs of failure disappear This may require more or less continued bed rest or inactivity for the remainder of the pregnancy If acute pulmonary edema occurs, it can be treated rapidly with morphine, phlebotomy, or rapid intravenous digitalization (pages 237 and 258)

Once compensation is restored, she can be allowed moderate physical activity, but should be admitted to the hospital at least two weeks, and preferably four weeks before the expected date of delivery.

Care of the Cardiac Patient in Labor.—All cardiacs should be delivered in a hospital.

First Stage of Labor—The cardiac who has never been in failure does not require prophylactic digitalization. However, the maternal pulse and respiratory rate should be taken every half hour because it has been noted that 50 per cent of the cases which show a pulse rate of 110 per minute or more and a respiratory rate of 24 per minute or more for over forty-five minutes during the first stage of labor, will develop failure. Under such circumstances, the patient should be rapidly digitalized.

Adequate analgesia with twilight sleep (morphine, 15 mg. [$\frac{1}{4}$ grain], and scopolamine, 0.4 mg. to 0 25 mg [$\frac{1}{150}$ to $\frac{1}{100}$ grain]) should be used during the first stage to prevent excess pain. The injections can be given as often as every four hours.

Second Stage of Labor.—Even if no cephalopelvic disproportion is present, the second stage should be eliminated by forceps as soon as the head is below the level of the ischial spines. While it is at or above this level, the patient may be allowed to bear down a few times while under ether analgesia so as to facilitate forceps delivery. Ether can be administered by the open-drip method, or with the closed method using adequate oxygen. Induction should be slow to prevent coughing, straining or vomiting.

If the patient is decompensated, she should be kept in a semiupright position during labor, and given oxygen as necessary.

Third Stage of Labor.—The third stage carries a small but definite risk for the cardiac patient, and the more or less sudden decrease in intra-abdominal pressure and the lowering of the diaphragm may cause circulatory disturbances and lead to collapse. For this reason, some obstetricians place three or four sandbags on the abdomen concurrently with the delivery of the child, and remove them one at a time at fifteen minute intervals

The use of ergotrate or pituitrin has been shown to raise the venous pressure even to abnormal levels during the early puerperium, and should not be used if possible. However, the uterus should be continually examined and massaged as often as necessary to keep it firm and to avoid bleeding

Care of the Cardiac Patient during the Puerperium.—As was pointed out above, failure may first appear during the puerperium, and a low-sodium diet should be continued. The mother should not be allowed to nurse the baby unless she has not been in heart failure and lactation should be suppressed

There has been a tendency recently to ambulate normal postpartum women even within twenty-four or thirty-six hours after delivery However, the postpartum with heart disease is entitled to at least a week of bed rest, even though she did not become decompensated during pregnancy

Sterilization.—If the poor-risk patient has not gone into heart failure, and desires to be sterilized, it can be easily done one to two days postpartum when the uterus is still in the abdomen, under local anesthesia However, it is preferable to allow three or four months to elapse and then do an abdominal sterilization

OTHER COMPLICATIONS OF RHEUMATIC HEART DISEASE DURING PREGNANCY

Thrombophlebitis.—Although thrombophlebitis is a common complication of pregnancy, even in normal women, it rarely causes embolic complications, and conservative therapy, with moderate rest, and the use of lukewarm, wet dressings, is beneficial Anticoagulants should not be used because of the danger of causing hemorrhage in the fetus. However, there is some evidence that anticoagulant therapy does not necessarily harm the fetus. Surgical ligation of the femoral veins (page 617) can be done if necessary

Paroxysmal Tachycardia.—This should be treated conservatively with syrup of ipecac (page 345), or sedatives or digitalis (page 348) Quinidine should not be used if possible because of its oxytocic effect.

Subacute Bacterial Endocarditis.—This should be vigorously treated with an appropriate antibiotic If there is a history of a healed subacute bacterial endocarditis, the patient should be warned against becoming pregnant again for at least six months. Otherwise fatal heart failure may occur The reason for this is that it apparently requires this time for the heart to regain its full strength. In addition, during labor, prophylactic penicillin (page 508) should be given to prevent a recurrence of the endocarditis

THE EFFECT OF PREGNANCY ON CONGENITAL HEART DISEASE

Rules similar to those described for rheumatic heart disease can be followed However, the type of congenital lesion must also be taken into account Patients with a patent ductus arteriosus, interauricular septal defect, interventricular septal defect, congenital a–v block, pulmonary stenosis, even the tetralogy of Fallot have been known to deliver spontaneously. However, patients with coarctation of the aorta may die from rupture of the aorta during the second stage of labor In general, patients with cyanotic congenital lesions should be advised not to become pregnant

During delivery, prophylactic treatment with penicillin (page 508) should be used to prevent subacute bacterial endocarditis, except in cases of auricular septal defect

THE EFFECT OF PREGNANCY ON HYPERTENSIVE CARDIOVASCULAR DISEASE

Women with essential hypertension are able to deliver spontaneously, although there is a greater danger of toxemia developing than in normal women In women with malignant hypertension, the prognosis is poor and pregnancy should be avoided However, sympathectomy done on such women has enabled them to have children subsequently, but even after sympathectomy, toxemia of pregnancy may develop

Essential hypertension should be differentiated from toxemia of pregnancy (pre-eclampsia and eclampsia) which appears in the second half of pregnancy and is usually characterized by marked generalized edema, the development of hypertension, albuminuria, and signs and symptoms due to either the hypertension or the retention of fluid within the body. Shortly after delivery the edema disappears and is followed in a variable period of time by the return of the blood pressure and urine to normal.

Toxemia can also be differentiated from ordinary hypertensive heart disease on ophthalmoscopic examination In toxemia, the retina shows a wet, glistening appearance (page 146). This is not specific for toxemia, but it does not occur in uncomplicated hypertensive heart disease

If essential hypertension develops during pregnancy, the rise in pressure occurs during the first half of pregnancy, whereas in toxemia, the rise in blood pressure occurs during the second half Thus, toxemia should be suspected in a pregnant woman who develops hypertension, albuminuria or a sudden gain in weight first in the fifth or sixth month or later

Hypertensive cardiovascular disease associated with coronary artery disease is fortunately rare in women of child bearing age, but cases of women who have spontaneously delivered after having suffered from a myocardial infarct have been reported.

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Chapter 50

SURGERY, ANESTHESIA, AND HEART DISEASE

Cardiac Contraindications to Elective Surgical Procedures.—The presence of heart disease itself is not necessarily a contraindication to surgery. Proof of this is evident in the extensive surgical procedures now being performed on patients with cyanotic congenital cardiac lesions, and on patients with malignant hypertension However, the presence of heart disease increases operative mortality to some extent, and a major surgical procedure should be done on a cardiac only after careful evaluation of the cardiovascular status of the patient.

Some of the more common complications that may occur to cardiacs during or after operation are shock due to blood loss or to vasodilatation due to the anesthetic agent, arrhythmias, such as paroxysmal tachycardia, cardiac standstill or ventricular fibrillation during the operation; postoperative thrombosis or embolism, including pulmonary embolism, acute pulmonary edema due to excess postoperative saline, blood or plasma infusions, or even myocardial infarction or acute myocardial anoxemia. While these complications also may occur in non-cardiacs, they are more prone to occur in patients with heart disease

There are at least seven cardiac contraindications to elective surgical procedures·

1 **Cardiac Decompensation.**—In cases of heart failure, regardless of the etiology of the underlying heart disease, an elective operation should be deferred until about three weeks after compensation is restored

2. **Acute Myocardial Infarction.**—Operation should be deferred until three or four months or longer after the acute infarct The presence of coronary artery disease with severe angina pectoris is also a contraindication to an elective major operation Minor surgical procedures can be done using local anesthesia with procaine, without epinephrine, which can precipitate an attack of angina pectoris or even myocardial infarction

3. **Acute Myocarditis or Pericarditis**—Acute myocarditis or pericarditis, whether rheumatic or due to some other etiology, should be allowed to subside before an elective operation is undertaken.

4 **Bacterial Endocarditis.**—This should be brought under control with antibiotic therapy before an elective surgical procedure is done

5. **Mitral Stenosis and Auricular Fibrillation.**—Although mitral stenosis and auricular fibrillation are not ordinarily contraindications to operation, the presence of a thrombus in the left auricle makes surgery dangerous because a fragment of the thrombus may break off during anesthesia as a result of the development of a rapid, irregular heart action, and even fatal embolism may result There is no way of predicting whether this will happen How-

ever, if the patient has previously had embolic phenomena, elective surgery is contraindicated

6. **Paroxysmal Tachycardia.**—Paroxysmal tachycardia of any type should be abolished if possible, or the ventricular rate slowed, before an elective operation is done.

7. **Syphilitic Aortic Insufficiency.**

The presence of bundle branch block, hypertension, or compensated valvular heart disease (with the exception of syphilitic aortic insufficiency) is not a contraindication to an elective surgical procedure. Even complete *a-v* block is not a contraindication to operation unless the patient has been suffering from syncopal attacks due to ventricular standstill

In considering cardiac complications to surgery, one must remember that the cardiac lesion may be partly or wholly produced by the condition requiring surgery. Thus, bacterial endocarditis may be engrafted on an arteriovenous fistula or a patent ductus arteriosus and can be cured quickly by excision of the fistula or ligation of the ductus Severe heart failure may result from an arteriovenous fistula or hyperthyroidism, and may require excision of the fistula or thyroidectomy to cure the decompensation. Similarly it may be impossible to eliminate edema and ascites in a patient with constrictive pericarditis until pericardiectomy is done.

Cardiac Contraindications to Emergency Surgical Procedures.—When a surgical emergency, such as purulent appendicitis, or a strangulated hernia with gangrene of the gut, or internal hemorrhage, or a saddle embolism of the aorta, *etc*, arises, it may be necessary to ignore the cardiac contraindications and operate on the patient, even in the presence of an acute myocardial infarction

Cardiovascular Complications Resulting From Anesthesia and Surgery.—Complications, such as shock, arrhythmias, and heart failure, can be controlled to a large degree by adequate preoperative care, choice of a suitable anesthetic, limiting the operation to essential procedures, and adequate postoperative care.

Preoperative Care.—Saline, blood, or plasma should be administered cautiously Instead of saline, 5 per cent glucose in distilled water can be used, and instead of whole blood, packed red blood cells, resuspended in 5 per cent glucose and distilled water, can be used In addition, the patient in failure should be adequately digitalized before operation. However, if an emergency operation must be performed, a phlebotomy of from 400 to 750 cc should be done, the blood being saved for possible use later; pleural effusions should be removed; and the operation done with continuous inhalation of 100 per cent oxygen. Rapid digitalization should also be used in such a case

Preoperative sedation should be adequate. Short-acting barbiturates should be given two hours preoperatively. Demerol, 50 mg, is preferable to morphine, because it depresses respiration less Morphine should not be given to patients over seventy years of age, and when used at all, should be combined with atropine or scopolamine in a ratio of 25:1 (15 mg. [$\frac{1}{4}$ grain] morphine to 0 6 mg. [$\frac{1}{100}$ grain] atropine or scopolamine)

Patients with coronary artery disease and angina pectoris can be given 0.5 gram ($7\frac{1}{2}$ grains) aminophylline and 30 mg. ($\frac{1}{2}$ grain) papaverine intra-

muscularly before operation; or 0 1 mg ($\frac{1}{600}$ grain) of nitroglycerin can be given sublingually every half-hour preoperatively, and even during the operation, if a local anesthetic is used

Choice of Operation.—The operative procedure used should be the one that entails minimal handling and trauma to tissues, minimal duration of anesthesia, and minimal loss of blood.

Choice of Anesthesia.—There is no perfect anesthesia for the cardiac patient, and it has been said with justification that the employment of a competent anesthetist using an anesthesia he is familiar with is more important than the actual anesthesia used. Ether is probably the best anesthesia for cardiacs. However, the following general comments can be made about the more common anesthetic agents

The depth of the anesthesia should be as light as possible For this reason, relaxant agents such as curare or flaxedil have been used

Curare—A solution of d-tubocurarine or intocostrin containing 20 mg (2 cc) can be given intravenously and repeated as necessary, to provide muscular relaxation in surgery without producing too deep anesthesia However, curare may produce temporary respiratory paralysis

Flaxedil.—This is a curare-like compound, containing 20 mg per cc for intravenous administration Its advantage over curare is that it has very little effect on the autonomic ganglia However, it can cause a tachycardia and is therefore contraindicated in patients with heart disease in whom tachycardia might be hazardous The average dose is 20 mg approximately every thirty minutes as required

Ether.—Ether is an excellent anesthesia because its action is well known, it usually does not produce dangerous cardiac arrhythmias, and it can be used in association with sufficient oxygen (more than 90 per cent) to prevent dangerous anoxemia

One disadvantage of ether is that a prolonged period of induction may occasionally be required If the induction is hurried, increased secretions in the respiratory tract may occur, along with cough, swallowing of ether-laden mucus and anoxia and carbon dioxide retention

Cyclopropane—Twenty per cent cyclopropane along with 80 per cent oxygen is an excellent anesthetic, but cyclopropane tends to stimulate the vagus, producing bradycardia and bronchospasm In addition, it may cause cardiac irritability with multiple ventricular premature contractions from varying foci, ventricular tachycardia, cardiac standstill and possibly ventricular fibrillation These arrhythmias can be aggravated if epinephrine is given to a patient under cyclopropane anesthesia

Cyclopropane has the following disadvantages

(*a*) It may produce bradycardia and bronchospasm due to parasympathetic stimulation and an increased vagal tone The electrocardiogram may show sinus arrest, nodal rhythm, or other signs of displacement of the primary pacemaker of the heart from the sinus node to the *a–v* node.

It has been shown that if atropine is given intravenously when a bradycardia of the nodal type is present during cyclopropane-ether anesthesia, and there is also carbon dioxide excess, the rhythm immediately changes to a ventricular rhythm with premature beats or tachycardia. However, if the excess carbon dioxide in the body is removed, the rhythm will revert

spontaneously to a sinus tachycardia. Therefore, if marked slowing of the heart occurs during cyclopropane anesthesia, one should oxygenate and hyperventilate the patient first and then inject atropine if the bradycardia persists.

(*b*) It may cause rapid rhythms by increasing the irritability of the myocardium Multiple premature ventricular contractions from varying foci, ventricular tachycardia, and rarely ventricular fibrillation may occur. This can be precipitated by an injection of epinephrine, which is therefore contraindicated if cyclopropane is used. However, during the excitement of the operation, the patient may liberate enough endogenous epinephrine to precipitate ventricular tachycardia. However, if small amounts of ether are mixed with the cyclopropane, this tendency can be averted to a large degree

(*c*) Cyclopropane shock This occurs at the conclusion of the anesthesia. One factor which produces it is respiratory acidosis which accompanies underventilation Therefore it can be prevented if an adequate respiratory exchange is maintained during the anesthesia. (It has been suggested that hypoventilation with an accumulation of carbon dioxide in the body is an important cause of cardiac arrest and hyperpotassemia, regardless of which anesthetic agent is used.)

Nitrous Oxide—Nitrous oxide can be used for induction, but anesthesia should not be maintained with it, because sufficient oxygen cannot be used.

Ethylene.—This is contraindicated in cardiacs also because sufficient oxygen can not be given Under no circumstances should the oxygen inhaled be allowed to drop below 20 per cent.

Spinal Anesthesia—A marked drop in blood pressure may occur with spinal anesthesia This makes it potentially dangerous in patients with hypertension or coronary artery disease, but allows its use in patients with heart failure, because the vasodilatation that occurs as a result of the anesthesia prevents acute pulmonary edema. The inhalation of 100 per cent oxygen can also be used during the anesthesia.

A drop in blood pressure and shock can be combatted during spinal anesthesia with pressor drugs such as neo-synephrine hydrochloride, or methedrine (d-desoxyephedrine hydrochloride, desoxyn). Neo-synephrine can be given intravenously in doses of 0 1 cc. to 0.3 cc. (1 to 3 mg.); or intramuscularly in doses of 0.1 cc. to 1 cc. (1 to 10 mg); or it can be used in the form of a continuous infusion during the operation, using 2 cc (20 mg.) dissolved in a liter of saline

Methedrine can be given in a dose of 1 cc. (20 mg.) intramuscularly, or 0.5 cc (10 mg.) intravenously, and repeated as necessary.

Pentothal Sodium.—Pentothal sodium is the most widely used intravenous anesthetic It is usually given in the form of a 2½ per cent solution It produces a slight increase in heart rate, vasodilatation and a moderate drop in blood pressure. When combined with the inhalation of 100 per cent oxygen, it is an excellent anesthetic for procedures lasting less than thirty minutes, even in patients with coronary artery disease.

If pentothal is given in large doses to obtain a deep plane of anesthesia, tachycardia and hypotension may develop. Inasmuch as pentothal (and the other barbiturates) are not analgesics, they do not block the sensory

pathways as readily as do most narcotics. As a result, afferent impulses from the operative site can reach the cerebral cortex and cause reflex spasm of the vocal cords with respiratory obstruction and anoxia, or reflex spasm of the abdominal muscles. If this happens, the dose of pentothal should not be increased because serious side-effects may develop. Instead, nitrous oxide can be given simultaneously, or a curare compound used to obtain muscular relaxation.

Local Anesthesia.—I dislike local anesthesia because the patient may become greatly frightened in the operating room.

Treatment of Cardiac Arrhythmias Developing during Anesthesia.—Cardiac arrhythmias are very common during inhalational anesthesia, especially with cyclopropane, but may also occur with intravenous anesthetics, such as pentothal sodium. The presence of a cardiac arrhythmia can be easily overlooked unless the patient is connected to a direct-writing electrocardiograph or to a cathode ray oscilloscope.

In general, two types of arrhythmias occur:

A. Abnormal rhythms such as nodal rhythm, *a–v* dissociation, sinus bradycardia, or sinus arrest, due to vagal depression of the sinus node. Such arrhythmias may also be produced by vagovagal reflexes initiated by endotracheal intubation, pulmonary hilar traction or bronchial or pericardial manipulation, or manipulation of the vagus nerve or intercostal nerves during intrathoracic operations.

Such arrhythmias usually disappear spontaneously, or after the intravenous administration of 0.6 mg. ($\frac{1}{100}$ grain) of atropine. However, if the heart rate remains below 50 in spite of the atropine, or if the bradycardia recurs, this may be a sign that terminal cardiac arrest is imminent.

B. Auricular, nodal, and ventricular premature contractions, and supraventricular and ventricular tachycardia, and even ventricular fibrillation can also be produced by anesthetic agents or manipulation of the heart, the pericardium or other intrathoracic organs.

Such arrhythmias can be stopped by the rapid intravenous injection of 100 mg. of procaine given in a 1 or 2 per cent solution. Topical application of 2 per cent procaine solution to the pericardium or heart, or infiltration of the hilar area with 5 to 10 cc. of a 1 per cent procaine solution may prevent such arrhythmias during intrathoracic surgery. Quinidine in a dose of 0.2 to 0.4 gram (page 346) or pronestyl (page 353) can also be given intravenously instead of the procaine.

If the electrocardiogram shows that a paroxysmal supraventricular tachycardia is present, a rapid intravenous injection of 8 cc. (1.6 mg.) lanatoside C (cedilanid) (page 258) or digoxin (page 258) will restore sinus rhythm.

It may also be advisable to change the anesthetic agent to ether.

Cardiac Arrest and Ventricular Fibrillation.—The heart may suddenly stop beating during anesthesia either due to cardiac arrest or ventricular fibrillation. Since the treatment of the two conditions is somewhat different, it is important to obtain electrocardiographic confirmation, if possible, because the fibrillatory waves may be so fine that they are not visible, but treatment should be started immediately and if possible within three minutes if life is to be restored, although cases of successful cardiac resuscitation have been reported even after forty minutes of cardiac asystole.

In either cardiac arrest or ventricular fibrillation, the anesthesia should be stopped immediately and endotracheal oxygen in 100 per cent concentration should be started immediately, along with manual massage of the heart with two hands, if possible. The diaphragm should be incised if necessary. Compression of the heart should be gradual, with abrupt relaxation, at about one-half the regular heart rate. The patient should be placed in the Trendelenburg position.

For cardiac arrest, 0.5 cc. of $\frac{1}{1000}$ epinephrine, diluted in 5 cc. saline, should be given intravenously. In a few minutes, half this dose can be injected into the right auricle or right ventricle. An infusion of 1 per cent procaine solution should also be started, because there is a tendency for epinephrine to produce ventricular fibrillation under these conditions.

For ventricular fibrillation, 5 cc. of a 1 per cent procaine solution should be painted over the surface of the heart, or injected into the right ventricle. *If a defibrillating apparatus is available, electrodes should be placed* on each side of the heart, and a shock of 110 volts and 1.5 amperes sent through the heart. It may be necessary to repeat the shock if the fibrillation does not disappear.

Since cardiac standstill develops after the ventricular fibrillation disappears, cardiac massage should be continued, and epinephrine can then be given.

Speed is urgent in the treatment of cardiac arrest because even if the patient is revived, he may never regain consciousness. Or, if he does, serious and permanent mental deterioration may result.

Postoperative Care.—Precautions against giving too much saline, blood or plasma must be observed as in the preoperative period. It may also be advisable to institute prophylactic anticoagulant therapy to avoid pulmonary embolism (see page 605). Pituitrin should not be used for postoperative distention in patients with hypertension because it may raise the blood pressure still further. The patient should be ambulated as soon as possible.

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Chapter 51

EMPLOYMENT AND HEART DISEASE

Can Patients with Heart Disease Work?—Patients with heart disease not only can work but many often do work in spite of their heart disease and in spite of the advice of the physician Actually, heart disease itself is not necessarily a contraindication to work. However, if severe congestive heart failure, acute myocardial infarction, acute carditis or acute pericarditis is present, even part-time work must be prohibited.

What Kind of Work Can the Cardiac Patient Do?—The answer to this question depends on the nature of the heart disease, and the responsibilities and dangers of various occupations, not only to the patient but to fellow workers, pedestrians, *etc.* For example, patients with recurrent attacks of paroxysmal tachycardia, or recurrent syncopal attacks due to a hyperactive carotid sinus reflex, aortic stenosis, postural hypotension or the Adams-Stokes syndrome, *etc*, can work if they will not endanger themselves or others during a syncopal attack. For this reason, persons so afflicted should not be allowed to drive a public conveyance. Similar restrictions hold for a patient with a healed myocardial infarct or angina pectoris. (However, a patient with a healed myocardial infarct should be permitted to drive his own automobile)

A serious cardiac condition is not necessarily a bar to even full-time employment, and many of my patients who have recovered from an attack of myocardial infarction or severe cardiac decompensation are now engaged as manual laborers, clerical workers or have returned to their professions. However, in the presence of coronary artery disease, or if there is a history of severe heart failure, occupations which involve severe physical exertion or straining or lifting of heavy objects should be avoided This may be difficult to accomplish especially if the patient's training or skill is limited and does not permit a wide choice of occupation In such cases, the availability of a community retraining and placement guidance program would be of great value in rehabilitation.

One of the problems which the physician must keep in mind when the patient who has recovered from cardiac disability asks, "When can I go back to work, and what kind of work can I do?" is that if the patient is restrained and limited too much, a severe and incapacitating cardiac neurosis may develop and prove to be a much more serious liability than the actual organic heart disease. In such cases, the physician may *have to* actively encourage the patient to resume his former occupation. However, the best treatment for a cardiac neurosis is to prevent it. In this connection I might mention that there has been a tendency on the part of the physician to underestimate the capacity of the heart for work, and to protect the

patient too much and for too long a period of time, especially in coronary artery disease (see page 608).

Another factor which should be kept in mind is that many patients with mild or moderate congestive heart failure or angina pectoris who are unable to work full-time can easily work part-time. However, in such cases the cooperation of the employer is necessary, and provision should be made for the patient to travel to and from work at such times when the public conveyances are least crowded.

A few generalizations can be made about the type of work suitable for cardiac patients. Cardiacs classified as having possible or potential heart disease or Class I A (see classification on page 123) can invariably be given unlimited activity. However, a patient with hypertensive heart disease, I A, should be warned against working on scaffolding or other high places. I A cardiacs with a rheumatic history should be told to avoid jobs in damp places or other jobs where risk of upper respiratory infections is greater than usual, for example, operating an elevator in a busy department store, or any other situation where one is exposed to crowds.

The majority of cardiacs diagnosed as I B, II B, and II C, can work forty hours a week in clerical and sales jobs and in most skilled and semiskilled occupations. Many III C cardiacs can be employed in sedentary or part-time jobs.

However, no set rules can be laid down. Each patient must be judged individually in terms of the functional capacity of his heart, his job, and his emotional reaction to his cardiac disability. Finally, in making a specific job recommendation, consideration must also be given to protecting other employees and the public.

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